

Supplementary data

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**Prevalence of ECG abnormalities and risk factors for QTc interval prolongation
in hospitalized psychiatric patients**

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Table S1. Characteristics of the 30 patients (37 ECGs) with prolonged QTc^a as indicated in Table 1 (male: ≥450 ms; female: ≥460 ms)

Gender	Age (years)	Heart rate (bpm)	QTc ^a (ms)	Drugs at known risk of TdP ^b	Drugs at possible risk of TdP ^b	Drugs at conditional risk of TdP ^b
Female	51	87	460	Escitalopram haloperidol,	Aripiprazole, torasemide	Quetiapine
Male	53	72	451	-	Olanzapine	Hydrochlorothiazide
Male	38	99	465	-	-	-
Male	63	78	451	-	Venlafaxine	Quetiapine
Male	35	91	474	Haloperidol, levomepromazine, methadone	Mirtazapine, venlafaxine	-
		78	455	Haloperidol, levomepromazine, methadone	Mirtazapine, venlafaxine	-
Male	63	85	453	Citalopram	-	-
Male	33	88	473	-	Buprenorphine, venlafaxine	Quetiapine
Male	49	100	452	Methadone	-	Quetiapine, ritonavir
Female	53	78	464	-	-	Quetiapine
		63	466	-	Olanzapine	-
Male	50	89	454	-	-	-
Female	53	77	473	Citalopram	-	Amisulpride
		79	467	Citalopram	-	Amisulpride, quetiapine
		91	469	Citalopram	-	Amisulpride, quetiapine
Male	57	63	474	Citalopram	Mirtazapine	-
Male	61	67	451	-	-	-
Female	52	69	497	-	Lithium	-
Female	43	76	466	-	-	-
Female	27	78	595	-	Lithium	Amisulpride
Female	62	55	463	Haloperidol	-	Sertraline
Male	29	64	487	-	-	-
Female	33	78	462	-	-	-
Female	39	78	460	Escitalopram	-	-
Female	40	88	466	Escitalopram	Risperidone	Diphenhydramine
Female	35	79	474	-	-	Hydroxyzine, quetiapine
Male	46	58	468	Domperidone	-	-
Female	56	68	469	Escitalopram	Risperidone	-
		68	477	Escitalopram	Risperidone	-
		72	490	-	Risperidone	Amisulpride
Female	26	61	465	-	-	Amisulpride
Male	30	99	451	-	Olanzapine	Quetiapine
Male	34	47	469	-	Mirtazapine	Quetiapine
Female	34	64	460	-	Lithium	Quetiapine
Male	28	58	470	Methadone	-	-
		81	458	Methadone	-	Quetiapine
Male	61	86	451	-	-	Quetiapine

bpm: beats per minute; TdP: torsades de pointes; ^a QTc: corrected QT interval using Bazett's formula for heart rates between 60-100 bpm and Fridericia's formula for heart rates <60 or >100 bpm; ^b according to www.crediblemeds.org.

Prevalence of ECG abnormalities

Bazett's correction formula (QTcB)

Among the 600 valid ECGs, an abnormality (as defined in **Table S2**) was detected in 18.5% of the ECGs (n=111), which corresponds to 18.9% of the stays (n=85) and 19.7% of the patients (n=78). A prolonged QTcB interval (≥ 450 ms for males; ≥ 460 ms for females) was observed in 9.8% of the patients (n=39), including a patient with a very high risk QTcB at 595 ms.

Table S2. Classification of the 78 patients (19.7%) with at least one abnormal ECG, among the 396 patients with at least one valid ECG

Description	Number of patients (%) ^a
Prolonged QTcB (male: ≥ 450 ms; female: ≥ 460 ms)	39 (9.8)
Repolarization abnormalities (excluding prolonged QTc and early repolarization)	23 (5.8)
Atrioventricular conduction disturbances (PR <100 ms; PR >200 ms)	10 (2.5)
Intraventricular conduction disturbances (QRS >120 ms)	5 (1.3)
Sinus bradycardia (<50 bpm)	13 (3.3)
Sinus tachycardia (>120 bpm)	2 (0.5)
Arrhythmias (premature beats; atrial fibrillation)	10 (2.5)
Remote myocardial infarction	3 (0.8)

QTcB: Bazett corrected QT interval; bpm: beats per minute; ^a more than one type of ECG abnormality possible per patient

Fridericia's correction formula (QTcF)

Among the 600 valid ECGs, an abnormality (as defined in **Table S3**) was detected in 13.5% of the ECGs (n=81), which corresponds to 14.2% of the stays (n=64) and 14.9% of the patients (n=59). A prolonged QTcF interval (≥ 450 ms for males; ≥ 460 ms for females) was observed in 2.8% of the patients (n=11), including a patient with a very high risk QTcF at 570 ms.

Table S3. Classification of the 59 patients (14.9%) with at least one abnormal ECG, among the 396 patients with at least one valid ECG

Description	Number of patients (%) ^a
Prolonged QTcF (male: ≥ 450 ms; female: ≥ 460 ms)	11 (2.8)
Repolarization abnormalities (excluding prolonged QTc and early repolarization)	23 (5.8)
Atrioventricular conduction disturbances (PR < 100 ms; PR > 200 ms)	10 (2.5)
Intraventricular conduction disturbances (QRS > 120 ms)	5 (1.3)
Sinus bradycardia (< 50 bpm)	13 (3.3)
Sinus tachycardia (> 120 bpm)	2 (0.5)
Arrhythmias (premature beats; atrial fibrillation)	10 (2.5)
Remote myocardial infarction	3 (0.8)

QTcF: Fridericia corrected QT interval; bpm: beats per minute; ^a more than one type of ECG abnormality possible per patient

Distribution and evolution of the QTc interval during hospitalization

Distribution of the QTc using Bazett's (QTcB) and Fridericia's (QTcF) correction formulas

Mean $\pm$ SD QTc interval in the 595 valid ECGs was 422 ± 24 ms (range 350-595) for QTcB and 403 ± 22 ms (range 348-570) for QTcF (see **Fig. S1**).

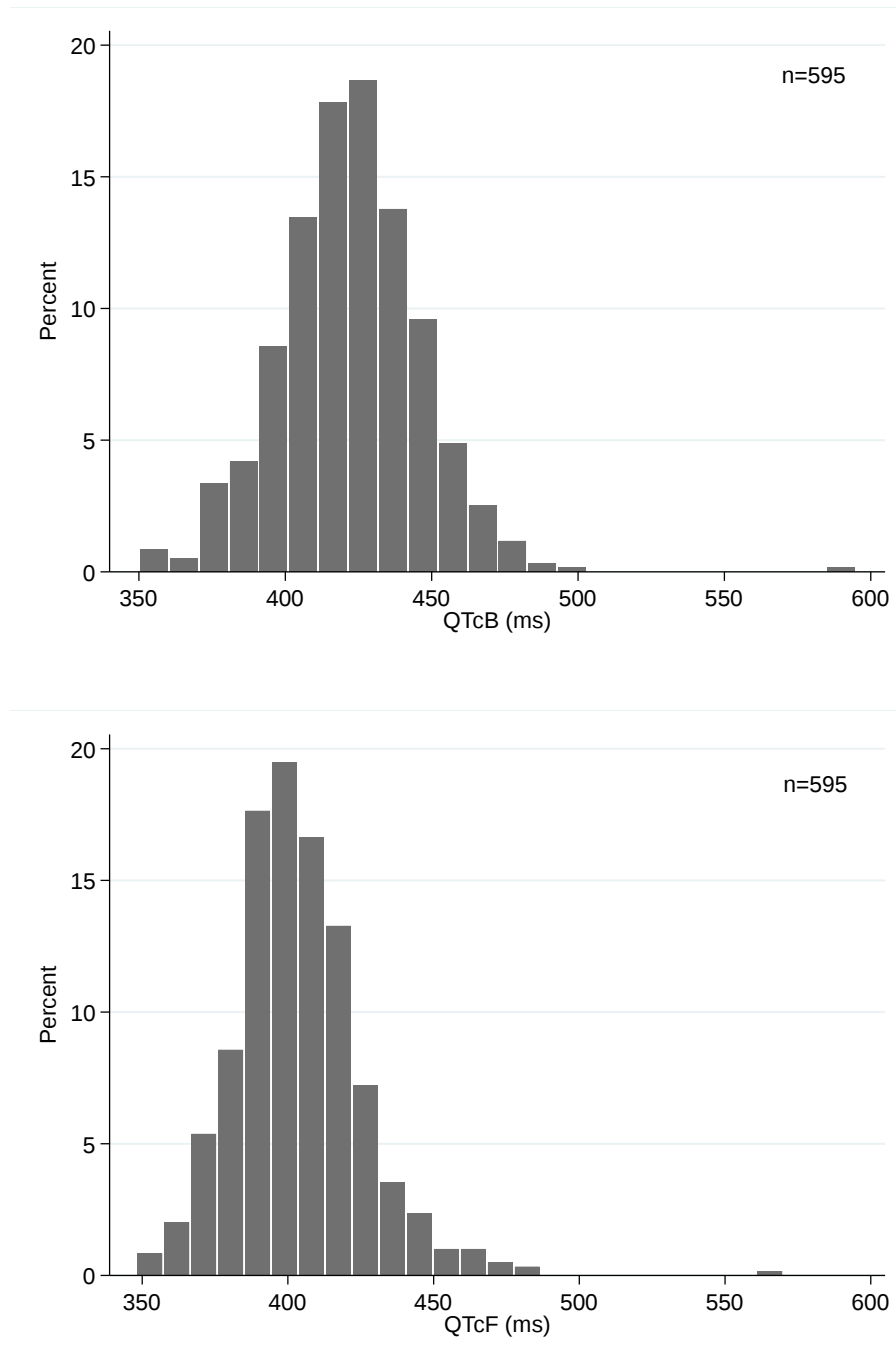


Figure S1. Distribution of the QTcB and QTcF values in the 595 valid ECGs.

Table S4. Characteristics of the 12 patients with a baseline QTc^a value in the upper quartile, among those having an ECG recorded within 48 hours after admission (baseline value) and another ECG between 3 and 30 days later (n=46)

Gender	Age (years)	Time to admission (days)	Heart rate (bpm)	QTc ^a (ms)	Difference of QTc between both ECGs	Drugs ^b (mg/d)	K ⁺ level (mmol/l)	Additional analyses/diagnoses
Female	44	1.1	93	448	1	Escitalopram (20), risperidone (3)	4.0	NA
		4.2	90	449		Escitalopram (20), risperidone (8)	NA	NA
Male	63	1.3	78	451	-17	Quetiapine (100), venlafaxine (225)	4.2	Diagnosis of alcohol dependence
		11.2	86	434		Aripiprazole (20), venlafaxine (225)	3.9	
Female	53	0.8	78	464	2	Quetiapine (350)	3.6	NA
		13.0	63	466		Olanzapine (30)	NA	NA
Female	57	0.8	79	458	-40	Escitalopram (10)	3.9	NA
		7.8	61	418		Escitalopram (10)	NA	NA
Female	62	1.0	74	445	-20	Quetiapine (150), sertraline (50)	3.3	NA
		7.8	59	425		Quetiapine (150), sertraline (50)	3.4 ^c	NA
Male	29	0.1	64	487	-118	Escitalopram (10), amisulpride (800)	NA	High amisulpride plasma level (542 ng/ml, ref. 100-320)
		19.0	51	369		Escitalopram (10), amisulpride (800)	NA	
Female	40	1.5	96	446	20	Paliperidone depot (100 mg/month)	4.2	NA
		16.6	88	466		Paliperidone depot (100 mg/month), diphenhydramine (50), escitalopram (5), risperidone (2)	NA	NA
Female	35	0.8	73	438	-20	-	4.1	Urinary screening positive for cocaine
		14.0	116	418		Quetiapine (100)	NA	
Female	56	1.1	68	469	-17	Escitalopram (20), risperidone (5)	3.8	NA
		7.1	67	452		Escitalopram (20), risperidone (5)	NA	NA
Female	54	2.0	99	457	-14	Olanzapine (20)	3.1	NA
		10.2	95	443		Olanzapine (20)	3.9	NA
Male	28	0.9	58	470	-65	Methadone (10)	4.3	Urinary screening positive for cocaine, opiates, methadone and THC
		16.6	83	405		Methadone (10), quetiapine (150)	NA	
Female	39	1.2	73	444	-20	Aripiprazole (15), fluoxetine (40)	NA	NA
		14.6	61	424		Amisulpride (400), sertraline (50)	4.1	NA

bpm: beats per minute; NA: not available; ^aQTc: corrected QT interval using Bazett's formula for heart rates between 60-100 bpm and Fridericia's formula for heart rates <60 or >100 bpm; ^b drugs at known, possible or conditional risks of torsades de pointes according to www.crediblemeds.org; ^c the day before the ECG.

Evolution of the QTc using Bazett's (QTcB) and Fridericia's (QTcF) correction formulas

The evolution of the QTc interval was studied in patients having an ECG recorded within 48 hours after admission (considered the baseline value) and another ECG between 3 and 30 days later (n=46). There were no significant differences between the two measurements for QTcB (mean $\pm$ SD: 424.2 ± 26.0 ms versus 422.3 ± 27.5 ms, $p=0.76$) and QTcF (403.8 ± 26.4 ms versus 400.8 ± 22.6 ms, $p=0.58$). When the proportion of patients with a QTc prolongation was considered, no significant change was observed between the two study periods for QTcB (10.9% versus 13.0%, $p=0.73$) and QTcF (4.3% versus 2.2%, $p=0.56$). However, in the patients with a baseline value in the upper quartile (n=12), a significant decrease was observed for QTcB (458.0 ± 13.3 ms versus 431.5 ± 30.3 , $p=0.03$) and QTcF (435.8 ± 21.9 ms versus 414.6 ± 24.3 ms, $p=0.03$). Similar results were obtained if cutoffs of 24 hours (n=28) and 72 hours (n=54) after admission were used for the baseline ECG (data not shown).

Risk factors for QTc prolongation

Risk factors for QTc prolongation using Bazett's (QTcB) and Fridericia's (QTcF) formulas

The covariates significantly associated with the QTcB interval in the multivariate model were (β , p): gender (+14.7 ms if female, $p<0.0001$), age (+0.3 ms/year, $p=0.008$), triglyceride plasma levels (+5.9 ms/mmol/l, $p=0.004$), glucose plasma levels (+2.9 ms/mmol/l, $p=0.018$), administration of at least one drug with known risk of torsades de pointes (+6.3 ms if ≥ 1 drug, $p=0.024$), administration of at least one drug with possible risk of torsades de pointes (+5.5 ms if ≥ 1 drug, $p=0.025$) and potassium plasma levels (-6.7 ms/mmol/l, $p=0.049$) (**Table S5**).

When the Fridericia's correction formula was used, the QTcF interval was significantly associated with gender (+14.3 ms if female, $p<0.0001$), age (+0.3 ms/year, $p=0.001$), triglyceride plasma levels (+6.3 ms/mmol/l, $p=0.001$) and administration of at least one drug with known risk of torsades de pointes (+6.6 ms if ≥ 1 drug, $p=0.007$), see **Table S5**.

Table S5. Linear mixed-effects model (357 ECGs, 313 stays, 292 patients)

Covariates	QTcB		QTcF	
	Beta ^a (ms)	<i>p</i>	Beta ^a (ms)	<i>p</i>
Females	+ 14.7	<0.0001	+ 14.3	<0.0001
Age (years)	+ 0.3	0.008	+ 0.3	0.001
Potassium (mmol/l)	- 6.7	0.049	- 3.0	0.30
Glucose (mmol/l)	+ 2.9	0.018	+ 0.41	0.67
Triglycerides (mmol/l)	+ 5.9	0.004	+ 6.3	0.001
Cholesterol total (mmol/l)	- 1.2	0.33	- 1.3	0.25
Creatinine (μmol/l)	+ 0.01	0.94	- 0.004	0.95
At least one drug with known risk of TdP ^b	+ 6.3	0.024	+ 6.6	0.007
At least one drug with possible risk of TdP ^b	+ 5.5	0.025	+ 1.8	0.39
At least one drug with conditional risk of TdP ^b	+ 4.2	0.08	+ 2.5	0.24
At least one strong CYP inhibitor ^c	+ 5.9	0.25	+ 6.4	0.14
At least one strong CYP inducer ^c	- 2.5	0.80	- 3.3	0.70
Time between admission and ECG (days)	- 0.1	0.22	- 0.1	0.24
F10-F19 ICD diagnosis	+ 1.7	0.55	+ 4.3	0.09

TdP: torsades de pointes; CYP: cytochrome P450; F10-F19 ICD diagnosis: mental and behavioral disorders due to psychoactive substance use; QTcB: Bazett corrected QT interval; QTcF: Fridericia corrected QT interval; ^a Effect of the covariate on the QTc; ^b Based on the classification of CredibleMeds (www.crediblemeds.org); ^c Based on the classification of the Geneva University Hospitals (www.pharmacoclin.ch).