Supplementary Table I. Post-marketing reports of QT prolongation and torsades de pointes after antidepressants

Drug	No. of reports	Adverse events	Reports by gender	Reports by age [years]
Citalopram hydrobromide[7]	36	ECG QT corrected interval prolonged (36)	Female (26), male (9)	20+ (26), < 20 (8)
Citalopram hydrobromide	196	Torsades de pointes (196)	Female (139), male (44)	20+ (178), < 20 (2)
Escitalopram oxalate	19	ECG QT corrected interval prolonged (19)	Female (14), male (4)	20+ (15)
Escitalopram oxalate	76	Torsades de pointes (76)	Female (53), male (18)	20+ (66), < 20 (3)
Venlafaxine hydrochloride	7	ECG QT corrected interval prolonged (7)	Female (6), male (1)	20+ (6), < 20 (1)
Venlafaxine hydrochloride	58	Torsades de pointes (58)	Female (43), male (14)	20+ (45), < 20 (2)
Desvenlafaxine succinate	0	ECG QT corrected interval prolonged (0)	Not reported	Not reported
Desvenlafaxine succinate	2	Torsades de pointes (2)	Female (2)	
Amitriptyline hydrochloride	14	ElCG QT corrected interval prolonged (14)	Female (9), male (5)	20+ (12), < 20 (2)
Amitriptyline hydrochloride	32	Torsades de pointes (32)	Female (24), male (7)	20+ (23), < 20 (8)
Bupropion hydrochloride	5	ECG QT corrected interval prolonged (5)	Male (4), female (1)	20+ (3), < 20 (1)
Bupropion hydrochloride	9	Torsades de pointes (9)	Female (6), male (3)	20+ (5), < 20 (4)
Duloxetine hydrochloride	12	ECG QT corrected interval prolonged (12)	Female (8), male (4)	20+ (9)
Duloxetine hydrochloride	4	Torsades de pointes (4)	Female (4)	20+ (3)
Fluoxetine hydrochloride	28	ECG QT corrected interval prolonged (28)	Female (19), male (7)	20+ (24), < 20 (2)
Fluoxetine hydrochloride	107	Torsades de pointes (107)	Female (90), male (12)	20+ (103)
Imipramine hydrochloride	5	ECG QT corrected interval prolonged (5)	Female (4), male (1)	20+ (4), < 20 (1)
Imipramine hydrochloride	5	Torsades de pointes (5)	Female (5)	20+ (4)
Paroxetine hydrochloride	3	ECG QT corrected interval prolonged (3)	Male (2)	< 20 (2)
Paroxetine hydrochloride	44	Torsades de pointes (44)	Female (31), male (9)	20+ (37)
Clomipramine hydrochloride	1	ECG QT corrected interval prolonged (1)	Female (1)	20+ (1)
Clomipramine hydrochloride	4	Torsades de pointes (4)	Female (2), male (1)	20+ (2), < 20 (1)

Supplementary Table I. Cont.

Drug	No. of reports	Adverse events	Reports by gender	Reports by age [years]
Dosulepin	No data	ECG QT corrected interval prolonged		
Dosulepin	No data	Torsades de pointes		
Fluvoxamine maleate	9	ECG QT corrected interval prolonged (9)	Male (5), female (4)	20+ (6), < 20 (3)
Fluvoxamine maleate	16	Torsades de pointes (16)	Female (12), male (4)	20+ (16)
Mirtazapine	13	ECG QT corrected interval prolonged (13)	Female (11), male (2)	20+ (13)
Mirtazapine	29	Torsades de pointes (29)	Female (19), male (9)	20+ (27)
Nortriptyline hydrochloride	2	ECG QT corrected interval prolonged (2)	Female (1), male (1)	20+ (2)
Sertraline hydrochloride	13	ECG QT corrected interval prolonged (13)	Female (8), male (5)	20+ (7), < 20 (3)
Sertraline hydrochloride	48	Torsades de pointes (48)	Female (23), male (16)	20+ (42), < 20 (3)
Trazodone hydrochloride	1	ECG QT corrected interval prolonged (1)	Female (1)	20+ (1)
Trazodone hydrochloride	20	Torsades de pointes (20)	Female (16), male (3)	20+ (18)
Selegiline hydrochloride	1	Torsades de pointes (1)	Female (1)	20+ (1)
Maprotiline hydrochloride	3	Torsades de pointes (3)	Female (2)	20+ (2)
Nefazodone hydrochloride	6	Torsades de pointes (6)	Female (6)	20+ (6)
Amoxapine	2	Torsades de pointes (2)	Female (2)	20+ (2)

From https://www.pharmapendium.com.

Supplemantary Table II. Observational studies that examined the association between citalopram with QT prolongation and related clinical outcomes

Active	Control	Outcome	Relative measure of association	Patients (studies)	Comment†
Citalopram > 40 mg	**Citalopram, 1–20 mg**	**Ventricular arrhythmias**	**Adjusted HR = 0.68 (0.61–0.76)**	**618,450 (1 observational study) [92]**	**Favors higher dose**
Citalopram > 40 mg	**Citalopram, 1–20 mg**	**All-cause mortality**	**Adjusted HR = 0.94 (0.90–0.99)**	**618,450 (1 observational study) [92]**	**Favors higher dose**
Citalopram > 40 mg	**Sertraline, high dose**	**Ventricular arrhythmias**	**RR = 0.77 (0.68–0.88)**	**245,787 (1 observational study) [92]**	**Favors citalopram**
Citalopram > 40 mg	**Sertraline, high dose**	**All-cause mortality**	**RR = 0.71 (0.68–0.75)**	**245,787 (1 observational study) [92]**	**Favors citalopram**
Citalopram dose reduce < 40 mg/day	**Citalopram > 40 mg/day**	**All-cause deaths or hospitalizations**	**Adjusted HR = 4.50 (4.10–5.00)**	**35,848 (1 observational study) [109]**	**Favors higher dose**
Citalopram dose reduce < 40 mg/day	**Citalopram > 40 mg/day**	**All-cause deaths or arrhythmia hospitalizations**	**Adjusted HR = 1.30 (1.00–1.70)**	**35,848 (1 observational study) [109]**	**Favors higher dose**
Citalopram, 20 mg	**Citalopram, 10 mg**	**QT prolongation**	**Adjusted MD = 9.80 (6.66–12.94)**	**38,397 (1 observational study) [86]**	**Favors lower dose**
Citalopram, 30 mg	Citalopram, 20 mg	QT prolongation	Adjusted MD = –0.90 (–6.19 – 4.39)	38,397 (1 observational study) [86]	No difference
Citalopram, 40 mg	Citalopram, 30 mg	QT prolongation	Adjusted MD = –0.70 (–6.19 – 4.79)	38,397 (1 observational study) [86]	No difference
Citalopram, 60 mg	**Citalopram, 40 mg**	**QT prolongation**	**Adjusted MD = 6.10 (1.98–10.22)**	**38,397 (1 observational study) [86]**	**Favors lower dose**

Boldface *indicates statistically significant differences at 95% CI.* †*We concluded that there is no difference in outcomes between active and control interventions based on p-value > 0.05 and inability to reject null hypotheses but without post hoc analysis of the statistical power to detect true differences.*

Supplementary Table III. GRADE summary of findings: effect of fluoxetine on QT interval in adults with mental disorders

Outcome	Risk with intervention per 1000	Risk with comparator per 1000	Relative measure of association	No. of participants (studies)	Quality (GRADE)	Comments†
QT prolonged, fluoxetine, 20 mg	6	4	RR = 1.54 (0.10–24.48)	427 (1 RCT) [114]	Very low	No difference
QT prolonged, fluoxetine, 40 mg	0	4	RR = 1.03 (0.04–25.09)	342 (1 RCT) [114]	Very low	No difference
QTC, ms	NR	NR	MD = 0.00 (–0.61 – 0.61)	54 (1 RCT) [46, 94]	Very low	No difference
Sudden death, with cardiovascular disease	NR	NR	Adjusted OR = 2.26 (0.96–5.34)	4040 (1 observational study) [76]	Low	No difference
Sudden death, without cardiovascular disease	NR	NR	Adjusted OR = 2.44 (0.77–7.74)	4040 (1 observational study) [76]	Low	No difference

Population: people with mental disorders; Settings: any; Intervention: fluoxetine; Comparator: placebo or no active drug. †*We concluded that there is no difference in outcomes between active and control interventions based on p-value > 0.05 and inability to reject null hypotheses but without post hoc analysis of the statistical power to detect true differences.*

Supplementary Table IV. GRADE summary of findings: effect of paroxetine on QT interval in adults with mental disorders

Outcome	Risk with intervention per 1000	Risk with comparator per 1000	Relative measure of association	No. of participants (studies)	Quality (GRADE)	Comments[†]
QT [ms]	NR	NR	MD = 6.80 (–3.96 – 17.56)	878 (6 RCTs) [39, 59, 69, 94]	Moderate	No difference
QTcB [ms]	NR	NR	MD =2.42 (–3.92 – 8.76), SMD = 0.13 (–0.22 – 0.48)	128 (1 RCT) [59]	Very low	No difference
QTcF [ms]	NR	NR	MD = 3.93 (–2.56 – 10.42), SMD = 0.21 (–0.14 – 0.56)	128 (1 RCT) [59]	Very low	No difference
QT [ms]	3	0	RR = 3.00 (0.12–73.33)	698 (2 RCTs) [59, 101]	Low	No difference
Sudden death, with cardiovascular disease	NR	NR	Adjusted OR = 1.42 (0.53–3.83)	4040 (1 observational study) [76]	Low	No difference
Sudden death, without cardiovascular disease	NR	NR	Adjusted OR = 0.20 (0.02–2.01)	4040 (1 observational study) [76]	Low	No difference

Population: adults with mental disorders; Settings: any; Intervention: paroxetine; Comparator: placebo or no active drug. [†]We concluded that there is no difference in outcomes between active and control interventions based on p-value > 0.05 and inability to reject null hypotheses but without post hoc analysis of the statistical power to detect true differences.

Supplementary Table V. GRADE summary of findings: effect of paroxetine on QT interval in children with mental disorders

Outcome	Risk with intervention per 1000	Risk with comparator per 1000	Relative measure of association	No. of participants (studies)	Quality (GRADE)	Comments[†]
Paroxetine vs. placebo:						
QT interval	NR	NR	MD = –4.40 (–9.46 – 0.66), SMD = –0.17 (–0.36 – 0.03)	407 (1 RCT) [68]	Very low	No difference
QTcB interval [ms]	NR	NR	MD = 0.70 (–3.59 – 4.99), SMD = 0.03 (–0.16 – 0.23)	407 (1 RCT) [68]	Very low	No difference
QTcF interval [ms]	NR	NR	MD = –1.20 (–4.85 – 2.45), SMD = –0.06 (–0.26 – 0.13)	407 (1 RCT) [68]	Very low	No difference
Maximum QTcB change from screening, 30–60 ms	**50**	**116 attributable avoided events per 1000 treated, 66 (13–119)**	**RR = 0.43 (0.21–0.88), NNTp = 15 (8–78)**	**407 (1 RCT) [68]**	**Very low**	**Favors paroxetine**
Maximum QTcB change from screening, > 60 ms	10	14	RR = 0.69 (0.12–4.09)	407 (1 RCT) [68]	Very low	No difference
Maximum QTcF change from screening, 30–60 ms	**25**	**116 attributable avoided events per 1000 treated, 91 (42–140)**	**RR = 0.22 (0.08–0.55), NNTp = 11 (7–24)**	**407 (1 RCT) [68]**	**Very low**	**Favors paroxetine**
Maximum QTcF change from screening, > 60 ms	0	14	RR = 0.15 (0.01–2.84)	407 (1 RCT) [68]	Very low	No difference

Supplementary Table V. Cont.

Outcome	Risk with intervention per 1000	Risk with comparator per 1000	Relative measure of association	No. of participants (studies)	Quality (GRADE)	Comments[†]
Absolute QTcB interval, > 440 ms	15	19	RR = 0.78 (0.18–3.42)	407 (1 RCT) [68]	Very low	No difference
Absolute QTcB interval, > 450 ms	10	14	RR = 0.69 (0.12–4.09)	407 (1 RCT) [68]	Very low	No difference
Absolute QTcB interval, > 480 ms	0	0	RR inestimable	407 (1 RCT) [68]	Very low	No difference
Absolute QTcB interval, > 500 ms	0	0	RR inestimable	407 (1 RCT) [68]	Very low	No difference
Absolute QTcF interval, > 440 ms	10	5	RR = 2.07 (0.19–22.65)	407 (1 RCT) [68]	Very low	No difference
Absolute QTcF interval, > 450 ms	5	5	RR = 1.04 (0.07–16.43)	407 (1 RCT) [68]	Very low	No difference
Absolute QTcF interval, > 480 ms	0	0	RR inestimable	407 (1 RCT) [68]	Very low	No difference
Absolute QTcF interval, > 500 ms	0	0	RR inestimable	407 (1 RCT) [68]	Very low	No difference
Paroxetine vs. imipramine:						
QTcB interval [ms]	**NR**	**NR**	**MD = –19.00 (–24.90 – –13.10) SMD = –0.94 (–1.28 – –0.59)**	**242 (1 RCT) [68]**	**Very low**	**Favors paroxetine**
QTcF interval, ms	**NR**	**NR**	**MD = –5.90 (–10.95 – –0.85) SMD = –0.33 (–0.66 – 0.01)**	**242 (1 RCT) [68]**	**Very low**	**Favors paroxetine**
Maximum QTcB change from screening, 30–60 ms	238	381	RR = 0.63 (0.32–1.21)	84 (1 RCT) [68]	Very low	No difference
Maximum QTcB change from screening, > 60 ms	48	119	RR = 0.40 (0.08–1.95)	84 (1 RCT) [68]	Very low	No difference
Maximum QTcF change from screening, 30–60 ms	**25**	**95**	**RR = 0.26 (0.07–0.94)**	**242 (1 RCT) [68]**	**Very low**	**Favors paroxetine**
Maximum QTcF change from screening, > 60 ms	0	24	RR = 0.07 (0.00–1.72)	242 (1 RCT) [68]	Very low	No difference
Absolute QTcB interval, > 440 ms	**15**	**190 attributable avoided events per 1000 treated, 175 (56–295)**	**RR = 0.08 (0.02–0.28), NNTp = 6 (3–18)**	**242 (1 RCT) [68]**	**Very low**	**Favors paroxetine**
Absolute QTcB interval, > 450 ms	10	48	RR = 0.21 (0.03–1.45)	242 (1 RCT) [68]	Very low	No difference
Absolute QTcB interval, > 480 ms	0	24	RR = 0.07 (0.00–1.72)	242 (1 RCT) [68]	Very low	No difference
Absolute QTcB interval, > 500 ms	0	0	RR inestimable	242 (1 RCT) [68]	Very low	No difference
Absolute QTcF interval, > 440 ms	10	24	RR = 0.42 (0.04–4.53)	242 (1 RCT) [68]	Very low	No difference
Absolute QTcF interval, > 450 ms	5	0	RR = 0.64 (0.03–15.49)	242 (1 RCT) [68]	Very low	No difference
Absolute QTcF interval, > 480 ms	0	0	RR inestimable	242 (1 RCT) [68]	Very low	No difference
Absolute QTcF interval, > 500 ms	0	0	RR inestimable	242 (1 RCT) [68]	Very low	No difference

Population: children with mental disorders; Settings: any; Intervention: paroxetine; Comparator: placebo or no active drug. **Boldface** *indicates statistically significant differences at 95% CI.* [†]*We concluded that there is no difference in outcomes between active and control interventions based on p-value > 0.05 and inability to reject null hypotheses but without post hoc analysis of the statistical power to detect true differences.*

Supplementary Table VI. GRADE Summary of findings: effect of bupropion on QT interval in adults with mental disorders

Outcome	Risk with intervention per 1000	Risk with comparator per 1000	Relative measure of association	No. of participants (studies)	Quality (GRADE)	Comments†
QT prolongation, bupropion vs. no antidepressants	NR	NR	Adjusted MD = –0.02 (–0.04 – 0.00)	38,397 (1 observational study) [86]	Low	No difference
QT prolongation, bupropion 100 mg vs. 75 mg	NR	NR	Adjusted MD = 0.00 (–4.12 – 4.12)	38,397 (1 observational study) [86]	Low	No difference
QT prolongation, bupropion, 150 mg vs. 100 mg	NR	NR	Adjusted MD = –3.30 (–7.61 – 1.01)	38,397 (1 observational study) [86]	Low	No difference
QT prolongation, bupropion, 200 mg vs. 150 mg	NR	NR	Adjusted MD = –1.80 (–5.92 – 2.32)	38,397 (1 observational study) [86]	Low	No difference
QT prolongation, bupropion, 300 mg vs. 200 mg	NR	NR	Adjusted MD –0.30 (–5.20 – 4.60)	38,397 (1 observational study) [86]	Low	No difference

Population: people with mental disorders; Settings: any; Intervention: bupropion; Comparator: placebo or no active drug. †We concluded that there is no difference in outcomes between active and control interventions based on p-value > 0.05 and inability to reject null hypotheses but without post hoc analysis of the statistical power to detect true differences.

Supplementary Table VII. GRADE summary of findings: effect of duloxetine on QT interval in adults with mental disorders

Outcome	Risk with intervention per 1000	Risk with comparator per 1000	Relative measure of association	No. of participants (studies)	Quality (GRADE)	Comments†
QTc value of > 500 ms 6 months, duloxetine, 80 mg	0	0	RR inestimable	128 (1 RCT) [59]	Very low	No difference
QTc value of > 500 ms 6 months, duloxetine, 120 mg	0	0	RR inestimable	132 (1 RCT) [59]	Very low	No difference
QT (ms) 2 months, duloxetine, 80 mg	NR	NR	MD = –0.27 (–0.56 – 0.02), SMD = –6.71 (–13.76 – 0.34)	186 (1 RCT) [59]	Very low	No difference
QTcB (ms) 2 months, duloxetine, 80 mg	NR	NR	MD = –0.06 (–0.34 – 0.23), SMD –0.88 (–5.45 – 3.69)	186 (1 RCT) [59]	Very low	No difference
QTcF (ms) 2 months, duloxetine, 80 mg	NR	NR	MD = –0.20 (–0.49 – 0.08), SMD = –2.91 (–7.00 – 1.18)	186 (1 RCT) [59]	Very low	No difference
QT (ms) 2 months, duloxetine, 120 mg	NR	NR	MD = –0.28 (–0.57 – 0.01), SMD = –7.45 (–15.11 – 0.21)	186 (1 RCT) [59]	Very low	No difference
QTcB (ms) 2 months, duloxetine, 120 mg	NR	NR	MD = 0.12 (–0.17 – 0.41), SMD = 2.48 (–3.57 – 8.53)	186 (1 RCT) [59]	Very low	No difference
QTcF (ms) 2 months, duloxetine, 120 mg	NR	NR	MD = –0.05 (–0.34 – 0.24), SMD = –0.97 (–6.55 – 4.61)	186 (1 RCT) [59]	Very low	No difference
QT (ms) 6 months, duloxetine, 80 mg	NR	NR	MD = –0.02 (–0.37 – 0.33), SMD = –0.63 (–10.58 – 9.32)	128 (1 RCT) [59]	Very low	No difference

Supplementary Table VII. Cont.

Outcome	Risk with intervention per 1000	Risk with comparator per 1000	Relative measure of association	No. of participants (studies)	Quality (GRADE)	Comments†
QTcB (ms) 6 months, duloxetine, 80 mg	NR	NR	MD = 0.24 (–0.11 – 0.59), SMD = 4.36 (–1.86 – 10.58)	128 (1 RCT) [59]	Very low	No difference
QTcF (ms) 6 months, duloxetine, 80 mg	NR	NR	MD = 0.15 (–0.20 – 0.50), SMD = 2.54 (–3.46 – 8.54)	128 (1 RCT) [59]	Very low	No difference
QT (ms) 6 months, duloxetine, 120 mg	NR	NR	MD = –0.03 (–0.38 – 0.31), SMD = –0.92 (–10.78 – 8.94)	132 (1 RCT) [59]	Very low	No difference
QTcB (ms) 6 months, duloxetine, 120 mg	NR	NR	MD = 0.04 (–0.31 – 0.38), SMD = 0.58 (–4.95 – 6.11)	132 (1 RCT) [59]	Very low	No difference
QT prolongation	NR	NR	Adjusted MD = 0.02 (–0.08 – 0.12)	38,397 (1 observational study) [86]	Low	No difference

Population: people with mental disorders; Settings: any; Intervention: duloxetine; Comparator: placebo or no active drug. †*We concluded that there is no difference in outcomes between active and control interventions based on p-value > 0.05 and inability to reject null hypotheses but without post hoc analysis of the statistical power to detect true differences.*

Supplementary Table VIII. GRADE summary of findings: effect of serotonin antagonist and reuptake inhibitors on QT interval in adults with mental disorders

Outcome	Risk with intervention per 1000	Risk with comparator per 1000	Relative measure of association	No. of participants (studies)	Quality (GRADE)	Comments†
Fluvoxamine:						
QTC [ms]	**NR**	**NR**	**MD = –5.00 (–6.04 – –3.96)**	**27 (1 RCT) [94, 149]**	**Very low**	**Favors fluvoxamine**
Sertraline:						
QTC [ms]	**NR**	**NR**	**MD = 3.00 (2.96–3.04)**	**369 (1 RCT) [50, 94]**	**Very low**	**Favors placebo**
Sudden death, with cardiovascular disease	NR	NR	Adjusted OR = 2.06 (0.57–7.47)	4040 (1 observational study) [76]	Low	No difference
Sudden death, without cardiovascular disease	NR	NR	Adjusted OR = 3.91 (0.62–24.62)	4040 (1 observational study) [76]	Low	No difference
Sertraline, high vs. low dose:						
Ventricular arrhythmias	**NR**	**NR**	**Adjusted HR = 0.70 (0.62–0.78)**	**365,898 (1 observational study) [92]**	**Low**	**Favors higher dose**
All-cause mortality	NR	NR	Adjusted HR = 1.00 (0.96–1.04)	365,898 (1 observational study) [92]	Low	No difference
Trazodone:						
QTc ≥ 450, adults with predialysis	NR	NR	Adjusted OR = 0.80 (0.40–1.50)	3252 (1 observational study) [112]	Low	No difference

Population: adults with mental disorders; Settings: any; Intervention: serotonin antagonist and reuptake inhibitors; Comparator: placebo or no active drug. **Boldface** *indicates statistically significant differences at 95% CI.* †*We concluded that there is no difference in outcomes between active and control interventions based on p-value > 0.05 and inability to reject null hypotheses but without post hoc analysis of the statistical power to detect true differences.*

Supplementary Table IX. GRADE summary of findings: effect of amitriptyline on QT interval in patients with mental or neurologic disorders

Outcome	Risk with intervention per 1000	Risk with comparator per 1000	Relative measure of association	No. of participants (studies)	Quality (GRADE)	Comments[†]
Children with functional gastrointestinal disorders:						
QTc	NR	NR	MD = –4.60 (–11.37 – 2.17), SMD = –0.28 (–0.70 – 0.13)	90 (1 RCT) [95]	Very low	No difference
Adults with diabetic peripheral neuropathy treated with amitriptyline 4% ketamine 2% cream:						
QT prolonged	0	9	RR = 0.33 (0.01–7.96)	226 (1 RCT) [78]	Very low	No difference
Adults with mental disorders:						
QT prolongation, amitriptyline vs. no antidepressants	**NR**	**NR**	**Adjusted MD = 0.11 (0.05–0.17)**	**38,397 (1 observational study) [86]**	**Low**	**Favors control**
QT prolongation, amitriptyline, 20 mg vs. 10 mg	NR	NR	Adjusted MD = –0.80 (–7.27 – 5.67)	38,397 (1 observational study) [86]	Low	No difference
QT prolongation, amitriptyline, 25 mg vs. 20 mg	NR	NR	Adjusted MD = 5.30 (–1.17 – 11.77)	38,397 (1 observational study) [86]	Low	No difference
QT prolongation, amitriptyline, 50 mg vs. 25 mg	**NR**	**NR**	**Adjusted MD = 3.40 (0.66–6.14)**	**38,397 (1 observational study) [86]**	**Low**	**Favors lower dose**
QT prolongation, amitriptyline, 75 mg vs. 50 mg	NR	NR	Adjusted MD = –2.00 (–8.47 – 4.47)	38,397 (1 observational study) [86]	Low	No difference
QT prolongation, amitriptyline, 100 mg vs. 75 mg	NR	NR	Adjusted MD = 1.90 (–6.14 – 9.94)	38,397 (1 observational study) [86]	Low	No difference
QTc ≥ 450, adults with predialysis CKD	NR	NR	Adjusted OR = 1.30 (0.80–2.20)	3252 (1 observational study) [112]	Low	No difference
Sudden death, with cardiovascular disease	NR	NR	Adjusted OR = 1.07 (0.48–2.40)	4040 (1 observational study) [76]	Low	No difference
Sudden death, without cardiovascular disease	NR	NR	Adjusted OR = 1.34 (0.54–3.43)	4040 (1 observational study) [76]	Low	No difference

Population: people with mental or neurologic disorders ; settings: Any; intervention: amitriptyline; Comparator: placebo or no active drug. **Boldface** *indicates statistically significant differences at 95% CI.* [†]*We concluded that there is no difference in outcomes between active and control interventions based on p-value > 0.05 and inability to reject null hypotheses but without post hoc analysis of the statistical power to detect true differences.*

Supplementary Table X. GRADE summary of findings: effect of imipramine on QT interval in children with mental disorders

Outcome	Risk with intervention per 1000	Risk with comparator per 1000	Relative measure of association	No. of participants (studies)	Quality (GRADE)	Comments†
QTcB interval [ms]	**NR**	**NR**	**MD = 19.70 (13.66–25.74), SMD = 0.88 (0.54–1.22)**	**249 (1 RCT) [68]**	**Very low**	**Favors placebo**
QTcF interval [ms]	NR	NR	MD = 4.70 (–0.33 – 9.73), SMD = 0.26 (–0.07 – 0.59)	249 (1 RCT) [68]	Very low	No difference
Maximum QTcB change from screening, 30–60 ms	**381**	**116 attributable events per 1000 treated, 265 (112–418)**	**RR = 3.29 (1.92–5.63), NNT = 4 (2–9)**	**249 (1 RCT) [68]**	**Very low**	**Favors placebo**
Maximum QTcB change from screening, > 60 ms	**119**	**14 attributable events per 1000 treated, 105 (5–204)**	**RR = 8.21 (2.04–33.06), NNT = 10 (5–190)**	**249 (1 RCT) [68]**	**Very low**	**Favors placebo**
Maximum QTcF change from screening, 30–60 ms	95	116	RR = 0.82 (0.30–2.24)	249 (1 RCT) [68]	Very low	No difference
Maximum QTcF change from screening, > 60 ms	24	14	RR = 1.64 (0.18–15.41)	249 (1 RCT) [68]	Very low	No difference
Absolute QTcB interval, > 440 ms	**190**	**19 attributable events per 1000 treated, 171 (51–291)**	**RR = 9.86 (3.11–31.24), NNT = 6 (3–20)**	**249 (1 RCT) [68]**	**Very low**	**Favors placebo**
Absolute QTcB interval, > 450 ms	48	14	RR = 3.29 (0.57–19.06)	249 (1 RCT) [68]	Very low	No difference
Absolute QTcB interval, > 480 ms	24	0	RR = 14.51 (0.60–350.26)	249 (1 RCT) [68]	Very low	No difference

Population: children with depression or obsessive-compulsive disorder; Settings: any; Intervention: imipramine; Comparator: placebo or no active drug. **Boldface** *indicates statistically significant differences at 95% CI.* †*We concluded that there is no difference in outcomes between active and control interventions based on p-value > 0.05 and inability to reject null hypotheses but without post hoc analysis of the statistical power to detect true differences.*

Supplementary Table XI. GRADE summary of findings: effect of tricyclic antidepressants on QT interval in adults with mental disorders

Outcome	Risk with intervention per 1000	Risk with comparator per 1000	Relative measure of association	No. of participants (studies)	Quality (GRADE)	Comments†
Clomipramine:						
Sudden death, with cardiovascular disease	NR	NR	Adjusted OR = 1.85 (0.11–30.20)	4040 (1 observational study) [76]	Low	No difference
Sudden death,without cardiovascular disease	NR	NR	Adjusted OR = 1.64 (0.16–17.24)	4040 (1 observational study) [76]	Low	No difference
Dosulepin:						
Sudden death, with cardiovascular disease	NR	NR	Adjusted OR = 2.11 (0.92–4.84)	4040 (1 observational study) [76]	Low	No difference
Sudden death, without cardiovascular disease	NR	NR	Adjusted OR = 1.65 (0.49–5.54)	4040 (1 observational study) [76]	Low	No difference
Fluvoxamine:						
QTC [ms]	**NR**	**NR**	**MD = –5.00 (–6.04 – –3.96)**	**27 (1 RCT) [94, 149]**	**Very low**	**Favors fluvoxamine**
Mirtazapine:						
QT prolongation	NR	NR	Adjusted MD = –0.13 (–0.29 – 0.03)	38,397 (1 observational study) [86]	Low	No difference
Nortriptyline:						
QT prolongation	NR	NR	Adjusted MD = 0.04 (–0.04 – 0.12)	38,397 (1 observational study) [86]	Low	No difference
Sudden cardiac arrest	**NR**	**NR**	**Adjusted OR = 4.60 (1.20–18.40)**	**5298 (1 observational study) [85]**	**Low**	**Favors control**

Population: adults with mental disorders; Settings: any; Intervention: tricyclic antidepressants; Comparator: placebo or no active drug. **Boldface** *indicates statistically significant differences at 95% CI.* †*We concluded that there is no difference in outcomes between active and control interventions based on p-value > 0.05 and inability to reject null hypotheses but without post hoc analysis of the statistical power to detect true differences.*