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QTc monitoring in adults with medical and psychiatric comorbidities: Expert consensus from the Association of Medicine and Psychiatry

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A B S T R A C T

Objective: Several psychiatric medications have the potential to prolong the QTc interval and subsequently increase the risk for ventricular arrhythmias such as torsades de pointes (TdP). There is limited guidance for clinicians to balance the risks and benefits of treatments.
Methods: After a review of the existing literature, clinical-educators from the Association of Medicine and Psychiatry developed expert consensus guidelines for ECG monitoring of the QTc interval for patients with medical and psychiatric comorbidities who are prescribed medications with the potential to prolong the QTc interval. A risk score was developed based on risk factors for QTc prolongation to guide clinical decision-making.
Results: A baseline ECG may not be necessary for individuals at low risk for arrythmia. Those individuals with a risk score of two or more should have an ECG prior to the start of a potentially QTc-prolonging medication or be started on a lower risk agent. Antipsychotics are not equivalent in causing QTc prolongation. A consensus-based algorithm is presented for the management of those identified at high (QTc > 500 msec), intermediate (males with QTc 450–499 msec or females with QTc > 470–499 msec), or low risk.
Conclusions: The proposed algorithm can help clinicians in determining whether ECG monitoring should be considered for a given patient. These guidelines preserve a role for clinical judgment in selection of treatments that balance the risks and benefits, which may be particularly relevant for complex patients with medical and psychiatric comorbidities. Additional studies are needed to determine whether baseline and serial ECG monitoring reduces mortality.

1. Introduction

Psychiatric medications, increased QTc interval, and associated risks including sudden cardiac death continue to attract clinical attention [1–3]. Since the voluntary withdrawal of the second-generation antipsychotic sertindole from the European market in 1998 due to concerns for increased risk of fatal ventricular arrhythmias, data has accumulated regarding risk of other psychopharmacological agents. In 2011, the United States Food and Drug Administration (U.S. FDA) identified the selective serotonin reuptake inhibitor (SSRI) citalopram as a potentially QTc-prolonging agent and recommended a maximum daily dose limit (40 mg) [4]. Although this warning was later revised, it

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served as a reminder that commonly prescribed medications may cause potentially dangerous alterations in ventricular repolarization.

Although imperfect, the QTc interval serves as a quantifiable marker for determining an individual's risk of developing potentially lethal ventricular arrhythmias; e.g., torsades de pointes (TdP). A major risk factor for the development of TdP is the addition, titration, or overdose of medication(s) (many of which have psychiatric indications) with potential to prolong the QTc interval. The U.S. FDA provides guidelines on reporting QTc changes for pharmaceutical industry drug development. Companies are required to conduct additional QTc monitoring for drugs in the early stage of development if initial results at therapeutic doses show an upper bound for increases in QTc ≥10 msec and at supratherapeutic doses show increases in QTc ≥10–20 msec [5].

The normal QTc interval of healthy individuals is generally around 400 msec, with sex-related differences such that QTc intervals in females are, on average, 20 msec longer than those in males, although this sex difference narrows after 40 years of age [1]. According to the American Heart Association and the American College of Cardiology, QTc over the 99th percentile should be considered abnormally prolonged [6]. Approximate 99th percentile QTc values for healthy individuals are 450 msec for males and 470 msec for females (Table 1) [7,8].

The American Heart Association has developed practice standards for in-hospital monitoring of the QTc interval [7]. The American Psychiatric Association also has a comprehensive resource guide for QTc monitoring in patients prescribed antipsychotics [9], We aim to augment other guidelines and resources by providing expert clinical consensus from the Association of Medicine and Psychiatry, with specific focus in patients with medical and psychiatric comorbidities and in clinical scenarios (e.g., outpatient mental health clinics) where access to ECG is limited. Despite current guidelines, there is a lack of consistent clinical application of ECG monitoring based on risks of individual medications of a particular class; for example, there is an overemphasis that “antipsychotics” as a class require ECG monitoring rather than evaluating each medication based on individual risk to prolong QTc [10]. In this article, we review the latest literature on QTc interval prolongation, detailing medications that represent the highest risk for QTc prolongation and TdP, especially in the outpatient settings. We propose practical clinical recommendations for monitoring risk, including appropriate use of the electrocardiogram (ECG), when prescribing these medications. We summarize our recommendations in an algorithm to guide clinical practice and future research efforts.

2. Methods

We conducted a PubMed database literature search for the period between 1990 and 2018, using the following keywords: “QTc prolongation,” “antipsychotic,” “QTc monitoring,”” torsades de pointes,” “antidepressant,” and “methadone.” A total of 88 articles were identified and included in preparation for the review. For medical disorders, using search terms of “QTc prolongation” and “risk factors” returned 362 articles under the category of clinical studies, 14 systematic reviews, and 60 articles in the category of medical genetics. Of the 436 articles identified by the search, 36 were selected and reviewed based on abstract content. We reviewed the latest society guidelines from the American Psychiatric Association, American Heart Association, American Pain Society and College on Problems of Drug Dependence and other clinical reviews not identified with our PubMed search. The Association of Medicine Psychiatry writing group for the review consists of academic clinician-educators from 12 U.S. institutions. Groups of 2–3 co-authors conducted keywords searches and generated initial drafts based on section topics. Another group of co-authors revised the combined drafts. Iterations of the drafts were completed over email discussions. A final video conference was held to resolve uncertainties and arrive at the expert consensus for the final manuscript.

Table 1
QTc length risk stratification based on gender.

QTc risk interpretation	Adult men (msec)	Adult women (msec)
Normal	≤ 430	≤ 450
Borderline	431–450	451–470
Prolonged	> 450	> 470

3. Results

3.1. Overview of risk factors for QTc prolongation

Etiologies of QTc prolongation may be divided into static and dynamic risk factors for prolongation of the QTc interval. *Static* risk factors include genetic abnormalities; e.g., Long-QT syndrome (LQTS). LQTS results from abnormalities in the potassium channels that are responsible for the repolarization of myocardium. Nearly 30% of individuals with acquired LQTS may carry genetic mutations for congenital LQTS [11]. This syndrome classically comes to attention when a young, otherwise healthy, individual suffers a cardiac event when participating in physical activity or sports. Historically, this familial abnormality was estimated to be quite rare at 1:5000 or even 1:20,000 births. However, more recent epidemiological studies have revised that estimation to 1:2000 births [12]. It is important for providers to attempt to identify patients with LQTS because their risk of sudden cardiac death are much higher when exposed to QTc-prolonging medications [13]. Beyond LQTS, quantitative data reveals nearly 50 characteristics that can come into play, including genetic alterations in hepatic metabolism of medications, body surface area, gender, cardiac output, and ion current permeability. The vast majority of these factors are not easily modifiable [14].

Dynamic risk factors for QTc prolongation include acute systemic medical illness, electrolyte abnormalities and medications (Table 2). Medication-associated QTc prolongation is thought to be mediated through the functioning of the delayed rectifier potassium ion channels [15]. In 2005, U.S. FDA issued guidance for premarketing investigation of the safety of new pharmaceutical agents to include information on the QT/QTc interval [16]. Based on evidence that TdP and life-threatening ventricular arrhythmias occur with QTc prolongation beyond 500 msec, QTc prolongation concerns are among the most common reasons a medication is either removed from the market or denied release by the U.S. FDA [17]; for example, sertindole is not available in the United States based on QTc interval prolongation > 500 msec in almost 8% of patients who took it [7].

Table 2
Risk factors for QTc prolongation.

Static (difficult to modify) risk factors	Dynamic (modifiable) risk factors
Congenital long-QT syndrome	Acute systemic illness
Sudden cardiac death in first degree family member	Hypokalemia
Age > 65 years	Hypomagnesemia
	Two or more QTc-prolonging agents
Female sex	
Structural heart disease (e.g., coronary artery disease, congestive heart failure)	
Underlying arrhythmia	
Personal history of unexplained syncope	

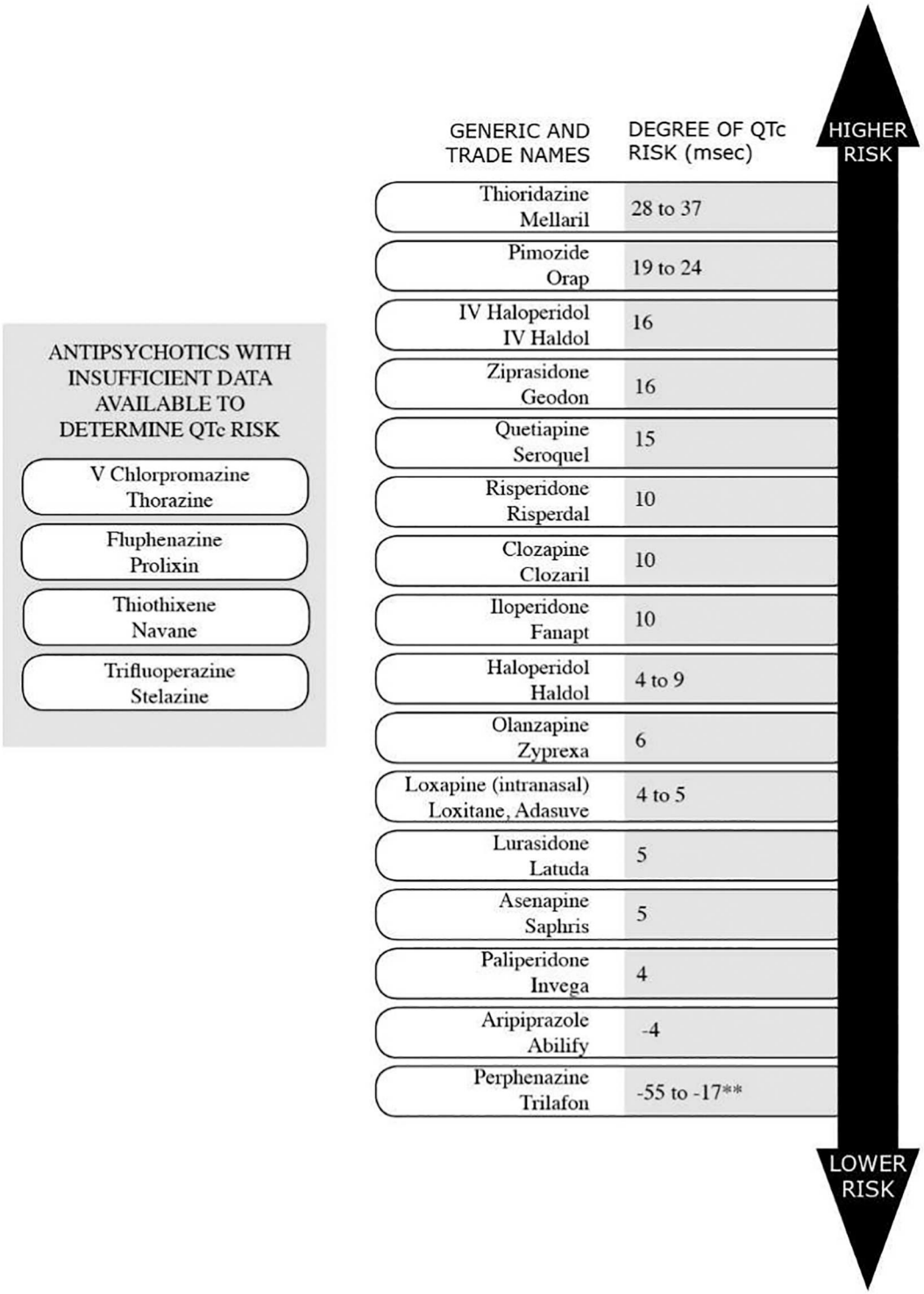

Fig. 1. Antipsychotic effect on QTc interval*.
* Based on data from references (15, 55, 69) unless otherwise specified.
Although reported values may demonstrate reduction in QTc, perphenazine use should still be treated with caution in patients with QTc prolongation.

3.2. Medical and patient-specific circumstances that increase the risk of QTc prolongation

3.2.1. Age

Age ≥ 65 years is the most common risk factor present in identified cases with QTc prolongation. In the 1991–2006 Swedish pharmacovigilance database, 72% of cases of QTc prolongation occurred in individuals over the age of 65 [18]. QTc interval lengthens as one ages for both men (mean QTc interval at age 50 = 405 msec; mean QTc interval at age 75 = 413 msec) and women (mean QTc interval at age 50 = 410 msec; mean QTc interval at age 75 = 415 msec) [19]. Factors that may contribute to a greater risk of QTc prolongation in older patients include reduced drug metabolism leading to higher drug levels, presence of cardiovascular disease that may not be clinically apparent, use of cardiovascular medications that may contribute to electrolyte abnormalities (e.g., loop diuretics), and presence of other medical co-

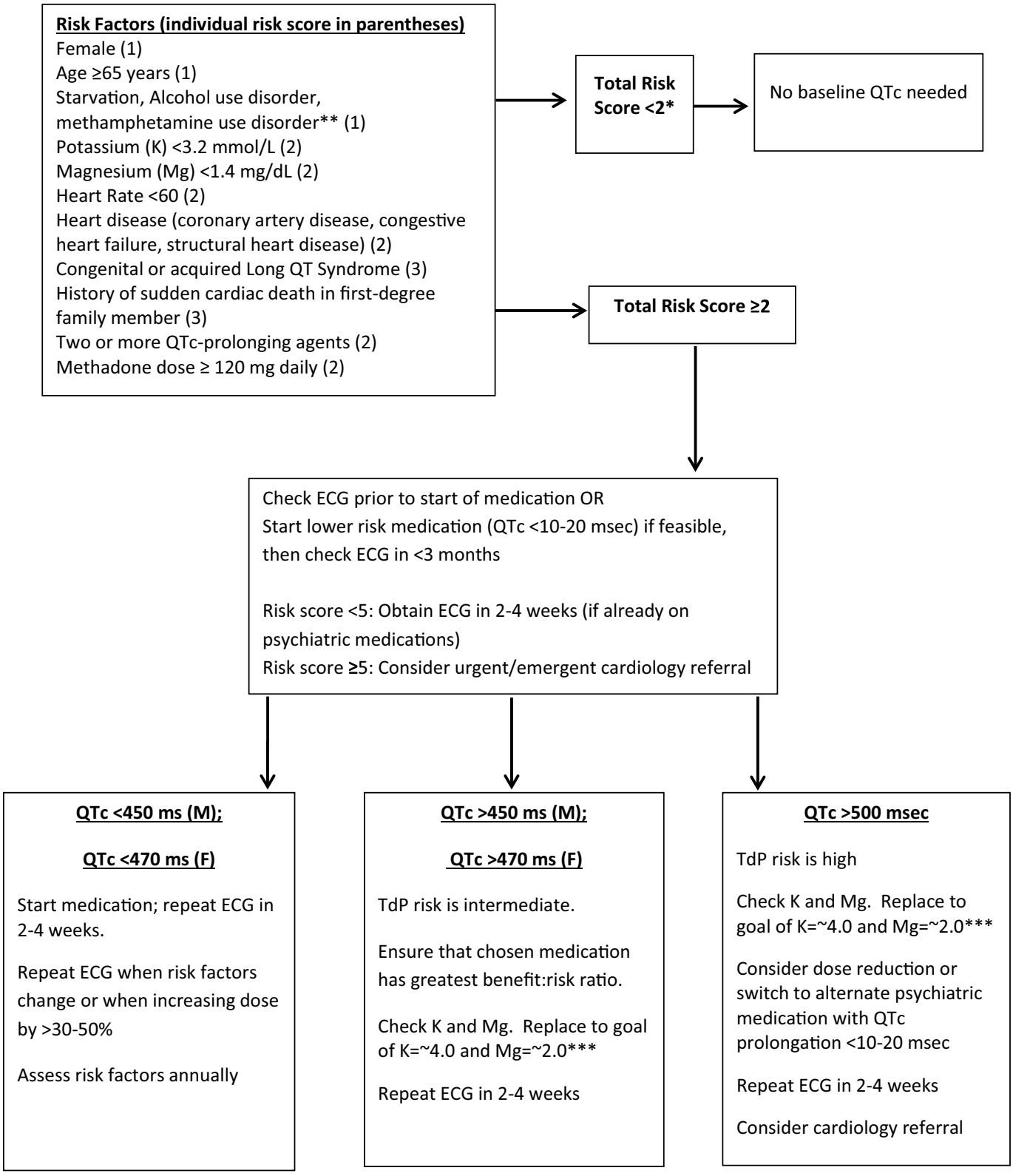

Fig. 2. Risk scoring and algorithm when starting and monitoring QTc-prolonging medications*.
* Refer to Fig. 1, and Tables 3 and 4 when considering individual medications that may not increase QTc by more than 10–20 msec. Not all antipsychotics may need to be included in this algorithm (e.g., aripiprazole).
**These conditions are often associated with electrolyte deficits such as hypokalemia and hypomagnesemia.
*** Potassium and magnesium levels are not evidence-based but based on clinical practice and associated risks as determined by consensus of the authors. Use clinical discretion to maintain potassium and magnesium levels to high normal or slightly above normal range.
Disclaimer: Note that the above recommendation is not based on randomized control study, but based on compilation of clinical data, medication-related QTc prolongation (as cited in the text) and the clinical consensus of the authors.

morbidities leading to additional QTc-prolonging agents [20].

3.2.2. Cardiovascular disease

The presence of cardiovascular disease will contribute to increased risk of TdP through direct physiologic relationships with abnormal anatomy (e.g., myocardial scarring predisposing to ventricular arrhythmias) and abnormal function (e.g., bradycardia) [21].

3.2.3. Sex

Female sex is the second most common risk factor associated with QTc prolongation, with 70% of QTc-prolonging cases in the Swedish database being female [18]. Reviews of case reports similarly show a 70% prevalence of TdP cases from psychiatric [22] and cardiovascular [23] medications occurring in females. The QTc interval decreases after puberty for males - but not females- suggesting an effect of sex hormones on ventricular repolarization [24]. Females also tend to have lower body mass and therefore high drug exposure per kilogram at the same dose; this discrepancy may be a possible underlying etiology since medications are not typically adjusted for body mass [25].

3.2.4. Electrolyte derangements

Electrolyte abnormalities, particularly hypokalemia, have been implicated in QTc prolongation and risk of TdP. As ventricular repolarization is predominantly mediated by delayed outward rectifier potassium currents (I_{Kr} and I_{Ks}), which are in turn dependent on extracellular potassium concentration, hypokalemia leads to decreased expression of these channels and thus prolonged ventricular repolarization [26].

3.3. Psychiatric medications that increase risk of QTc prolongation

3.3.1. Antipsychotics

Antipsychotic medications have long been associated with a dose-dependent risk of QTc prolongation and sudden death [27]. In 1991, Mehtonen et al. surveyed three years of autopsy data associated with sudden deaths and identified 49 unexpected deaths associated with psychotropic medications. Low-potency phenothiazines were documented in all but three of the 49 deaths, and thioridazine was implicated in over half. In 1996, the second generation antipsychotic sertindole was linked to 12 sudden unexplained deaths due to malignant arrhythmias and was, therefore, denied registration in the U.S. In 2000, a boxed warning was added to the U.S. FDA package insert for thioridazine, outlining heightened risk of sudden death due to TdP. Overall, first- and second-generation antipsychotics are associated with similar rates of sudden cardiac death and in a dose-dependent manner [28]. Pimozide is associated with an increase of 19 to 24 msec and is rarely used in clinical practice [29]. Ziprasidone represents the next highest risk with the potential to add 15.9 msec to baseline QTc interval [30], while aripiprazole appears to be least likely to cause significant QTc interval prolongation. There is insufficient information on newer antipsychotics; e.g., brexpiprazole and cariprazine. See Fig. 1 for additional details about other antipsychotics commonly used in clinical practice [17].

Medication route of administration and clinical indication for that administration may influence the degree of QTc prolongation, which also is dose-dependent for two butyrophenones, haloperidol and droperidol, that carry boxed warnings from the FDA regarding risk of QTc prolongation. QTc prolongation with intravenous haloperidol is likely higher when compared to oral formulation (although there are no direct comparative studies that we are aware of); there's higher risk from higher doses [31]. The U.S. FDA accordingly recommends placing any patient prescribed intravenous haloperidol on a cardiac monitor given the high risk of QTc prolongation [32]. Low doses of intravenous haloperidol (4 mg/day), which may frequently be used in intensive care unit settings, have not been associated with a particularly increased risk of TdP [33]. Higher doses (with an apparent threshold effect at 35 mg per day) have been associated with an increased risk of TdP [34]. Similarly, droperidol is utilized in many emergency settings for the treatment of acute agitation and also has a boxed warning regarding risk of QTc prolongation. A systematic review of studies evaluating droperidol's effect on QTc demonstrated that droperidol is associated with about the same risk of QTc prolongation as other anti-agitation medications at intramuscular or intravenous doses of up to 10 mg [35].

It is important to keep in mind that as many as 75% of TdP cases occur at therapeutic doses of antipsychotic medications [36]. The risk of TdP is highest with QTc prolongation > 500 msec, though of 28 cases of TdP, six (21.4%) experienced it with a QTc interval < 500 msec [36]. Importantly, the risk of TdP is strongly associated with additional risk factors – drug-associated QTc interval prolongation by itself rarely is reported to cause TdP. In fact, at least one additional well-established risk factor for QTc prolongation was present in 92.2% of case reports [37]; for example, ziprasidone is associated with the highest degree of QTc prolongation among the second-generation antipsychotics at 16 msec. However, there only are isolated reported cases of ziprasidone-induced TdP in patients who also have multiple additional risk factors for QTc interval prolongation [37,38]. Other second-generation antipsychotics; e.g., risperidone and quetiapine, which can prolong QTc interval by about 10 msec and 14 msec respectively, are rarely reported to cause TdP or sudden death. One study found only 15 cases of risperidone-induced QTc prolongation or TdP in a 20-year span [39]. A similar analysis of quetiapine-induced events identified only 12 incidents in a 14-year span [36]. In both analyses, several patients were found to have had multiple other risk factors for QTc interval prolongation. Even for intravenous haloperidol, Meyer-Massetti et al. reported that 68 out of 70 of the identified cases of QTc interval prolongation or TdP were determined to have additional associated risk factors [40].

3.3.2. Antidepressants

In August 2011, the U.S. FDA issued a boxed warning for citalopram related to prolongation of the QTc interval and resulting concern for potentially fatal arrhythmias. This announcement, regarding what previously had been considered to be a fairly benign drug, reawakened awareness regarding potential effects of medications on QTc [41]. The evidence to date suggests that citalopram (which increases QTc by about 10–20 msec) and escitalopram (which increases QTc by about 5–11 msec) carry the highest risk of QTc prolongation among second-generation antidepressants (e.g., selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors), while most other antidepressants have negligible effects on QTc [42].

3.3.3. Methadone

Methadone is a long-acting opioid medication used for a subset of patients with pain or severe opioid use disorder and no specific contraindications to opioid agonist treatment. The recommended initial daily dose ranges from 10 to 30 mg with dose increases in 5–10 mg/day increments no more frequently than every 7 days. Usual daily treatment dosages range from 60 to 120 mg, typically administered once a day for opioid replacement therapy [43]. Treatment of chronic pain is accomplished in similar total daily doses divided 3–4 times daily.

Although one study looking at initiation of low dose methadone for chronic pain suggests that QTc prolongation is rare and is negligible by 3 to 6 months after initiation of treatment, other studies point to a stronger and more durable association between methadone and QTc prolongation [44]. The largest cross-sectional study to date showed a dose-dependent QTc prolongation with oral methadone treatment, estimating a 10 msec increase in QTc for every 50 mg daily dose increase in methadone dose, which also corresponded to a higher risk for syncope [24].

Several studies assessed prevalence in various populations of QTc prolongation in patients receiving methadone for cancer-related pain [45–47]. The highest prevalence was 16% in one study [45] but no

Table 3
Antidepressant effect on QTc interval.

Generic name	Trade name	Degree of QTc risk milliseconds (ms)
Selective Serotonin Reuptake Inhibitors (SSRI)		
Citalopram	Celexa	10-20 ms
Escitalopram	Lexapro	5-11 ms
Fluoxetine	Prozac	Negligible effect
Fluvoxamine	Luvox	Negligible effect
Paroxetine	Paxil	Negligible effect
Sertraline	Zoloft	Negligible effect
Serotonin and Norepinephrine Reuptake Inhibitors (SNRI)		
Desvenlafaxine	Pristiq	Negligible effect [59]
Duloxetine	Cymbalta	Negligible effect
Venlafaxine	Effexor	Negligible effect [60]
Milnacipran	Savella	None reported/data insufficient
Levomilnacipran	Fetzima	None reported/data insufficient
Tri/tetra-cyclic Anti-depressants (TCA)		
Amitriptyline	Elavil	1-20 ms
Desipramine	Norpramin	11-24 ms
Doxepin	Silenor	8-22 ms
Imipramine	Tofranil	4-20 ms
Nortriptyline	Pamelor	Negligible effect
Amoxapine	Asendin	None reported/data insufficient
Clomipramine	Anafranil	−1.6-14.7 ms
Maprotiline	Ludiomil	Significant effect 20-40 ms
Trimipramine	Surmontil	15-20 ms [61]
Protriptyline	Vivactil	None reported/data insufficient
Mianserin	Tolvon	−10.3–6.9 ms [62]
Monoamine Oxidase Inhibitors (MAOI)		
Phenelzine	Nardil	Negligible effect [63]
Selegiline	Eldepryl	Negligible effect [64]
Tranylcypromine	Parnate	Negligible effect [65]
Atypical anti-depressants		
Bupropion	Wellbutrin	Negligible effect
Mirtazapine	Remeron	Negligible effect
Nefazodone	Serzone	Negligible effect [66]
Trazodone	Desyrel	- 4-7 ms
Vilazodone	Viibryd	Negligible effect [67]
Vortioxetine	Trintellix	None reported/data insufficient

*Based on references (42, 62, 68) and others as specifically cited.

increase risk in another study with mean methadone dose of 27.0 ± 24.3 mg/d in pediatric patients [47]. Studies assessing assisted treatment of opioid dependence and QTc prolongation estimate a 16.2% prevalence of QTc prolongation among patients prescribed methadone [48].

3.3.4. Polypharmacy

Polypharmacy also represents a risk factor for QTc prolongation via the concurrent administration of multiple drugs that may adversely influence ventricular repolarization through either pharmacokinetic or pharmacodynamic mechanisms. A retrospective review of outpatient pharmacy administrative claims revealed that 22.8% of subjects filled prescriptions for medications known to cause QTc prolongation, 9.4% filled overlapping prescriptions for two or more QTc-prolonging drugs or for a QTc-prolonging drug and another drug that inhibits its clearance, and 0.7% filled overlapping prescriptions for three or more of these drugs. Of the patients filling overlapping prescriptions, 22% were aged 65 or older and 74% were women, representing additional risk factors for QTc prolongation and the development of TdP [1].

3.3.5. Association with TdP and sudden cardiac death

More than 70–85% of reports of drug-induced QTc prolongation occur in patients who have two or more risk factors [15,49]. A recent systematic review evaluated pooled data on significant drug-associated QTc prolongation and rates of arrythmias attributed to prolonged QTc. The review identified 176 candidate studies, of which 36 assessed at least four cases with available information about drug-induced QTc prolongation (including ECG readings, drug dosing, and reported arrhythmias including TdP and sudden cardiac death [SCD]). Of the 14,756 patients included in the analysis, 930 (6%) exhibited QTc prolongation. Non-sustained ventricular tachycardia, pre-ventricular contractions and ectopy were the most common arrythmias associated with prolonged QTc in 379 patients (2.6%). TdP was reported in 49 patients (0.33%), and SCD was reported in five total patients. The authors found that the most significant risk factor for QTc prolongation was the use of multiple QTc-prolonging antipsychotic drugs; increased mortality was likely with polypharmacy, particularly with agents such as azithromycin, methadone, sertindole, amiodarone, sotalol and/or dofetilide [50].

Table 4
Common (non-psychiatric) medications associated with prolonged QTc.

Medication or class	Examples
Antiarrhythmics	Amiodarone, flecainide
Antihistamines	Hydroxyzine
Fluconazole	
Fluoroquinolones	Ciprofloxacin, levofloxacin
Macrolides	Azithromycin, clarithromycin, erythromycin
Methadone	
Ondansetron	

3.3.6. Management

Concern about QTc prolongation needs to be balanced with the risk of an untreated psychiatric illness or psychiatric decompensation. In addition to ECG monitoring, patients prescribed agents with potential to prolong the QTc interval should also be monitored for electrolyte disturbances, specifically hypokalemia and hypomagnesemia [51]. Patients with severe diarrhea or vomiting, with alcohol use disorder, and receiving certain medications; e.g., loop and thiazide diuretics also may be at increased risk for relevant electrolyte disturbances and should undergo electrolyte monitoring [52,53].

The decision to prescribe antipsychotic therapy should be based on a comprehensive risk versus benefit assessment, with appropriate informed consent, in a patient whose comprehensive medical and medication history is known by the prescriber. The “two or more additional risk factors” rule should be taken into consideration when conducting ECG monitoring. In hospital settings, QTc monitoring is recommended before initiation or dose adjustment of QTc-prolonging agents, with follow-up ECG 8 to 12 h thereafter [7]. While we are in agreement with this guideline, we recognize that the majority of patients taking psychiatric medications are seen in outpatient settings, and often in community mental health programs where ECG may not be routinely available.

According to a recent resource document published by the American Psychiatric Association Guidelines, healthcare providers should obtain a thorough medical and medication history and baseline ECG (within 1 month) prior to initiation of antipsychotics [6]. However, the absence of baseline ECG should not preclude antipsychotic prescription. There is no QTc interval for which antipsychotics are absolutely contraindicated. In patients with marked QTc interval prolongation (> 500 msec) or a sudden increase of QTc interval (> 60 msec from baseline), both of which are circumstances associated with a higher risk of TdP, changing (or reducing the dosage of) the medication and work-up for electrolyte abnormalities should be pursued [1,2,6].

American Pain Society guidelines recommend against using methadone in patients with a baseline QTc interval > 500 msec, and they also recommend follow-up ECG with each dose escalation of 30–50% higher than the previous dose at which ECG was obtained. In patients who are found to have significant QTc prolongation thought to be related to methadone treatment, clinicians can consider reducing the methadone dose or discontinuing methadone with follow up ECG to demonstrate improvement in QTc [53,54]. If continued opioid agonist treatment is required for the treatment of opioid addiction, clinicians

may consider a transition to buprenorphine [55–57]. Recent clinical practice guidelines from the American Pain Society and College on Problems of Drug Dependence suggest baseline ECG within 3 months *prior* to the initiation of methadone in patients with risk factors for QTc prolongation, any prior ECG demonstrating a QTc > 450 msec, or a history suggestive of prior ventricular arrhythmia [58].

We recommend a stepwise approach in calculating a risk score, starting QTc-prolonging medications, and monitoring QTc in Fig. 2 and, when possible, avoiding concurrent use of other QTc-prolonging "non-psychiatric" medications, especially methadone. At the present, no studies have demonstrated that obtaining baseline and serial ECG lowers mortality. The proposed algorithm is no different and requires further refinement. Randomized controlled studies large samples size and multiple medications may not be feasible, but prospective studies with high risk medications in high risk populations should be conducted.

3.4. Summary recommendations

3.4.1. Patient assessment and selection

- When considering initiation of medication with the potential to prolong the QTc interval, consider risk factors for QTc prolongation: age ≥ 65, cardiovascular history, electrolyte abnormalities (especially magnesium and potassium), clinical conditions with high risk of electrolyte abnormalities especially substance use disorder, and polypharmacy.
- When baseline QTc is not immediately possible, psychiatric medications with known high risk of significant QTc prolongation (e.g., high dose intravenous haloperidol, thioridazine, ziprasidone, citalopram) should be avoided in favor of psychiatric medications with lower QTc prolongation (< 10 msec (Table 3 and Fig. 1)).
- Review other medications that may prolong QTc (Table 4).

3.4.2. Baseline ECG

- Baseline and follow-up ECG should be obtained whenever feasible for patients with two or more risk factors or any prior ECG demonstrating a QTc > 450 msec in male or > 470 msec in female patients (Fig. 2).
- An ECG within the previous 3–6 months in patients without new risk factors for QTc interval prolongation can be used for the baseline study, if there are no new medical conditions.
- Since patients may ultimately be exposed to multiple psychiatric medications, ECG should be obtained when possible (especially in inpatient settings) and recorded in the medical record.
- In mental health clinics where ECG is not available, clinicians should work with clinic administrators to make ECG and laboratory services available onsite and/or to create useful collaborations with primary care clinics for such services.

3.4.3. Follow-up ECG

- Clinicians should, after a careful weighing of risk and benefits, strongly consider discontinuing, lowering, or switching therapy involving a medication linked to QTc prolongation or TdP when the follow-up QTc interval is > 500 msec or there is an increase of > 60 msec in the QTc interval compared with the prior pre-drug baseline value.

3.4.4. Patient education

- Patients in acute need of antipsychotic medications may not always be fully able to participate in detailed discussions about risk/benefit and rationale, and medications should be selected in an effort to minimize harms and maximize therapeutic effect. Risks and implications of QTc prolongation should be discussed in detail with the patient and/or proxy decision-maker as soon as feasible, and an informed discussion about static and modifiable risk factors and recommendations for monitoring should be undertaken for shared decision-making.

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