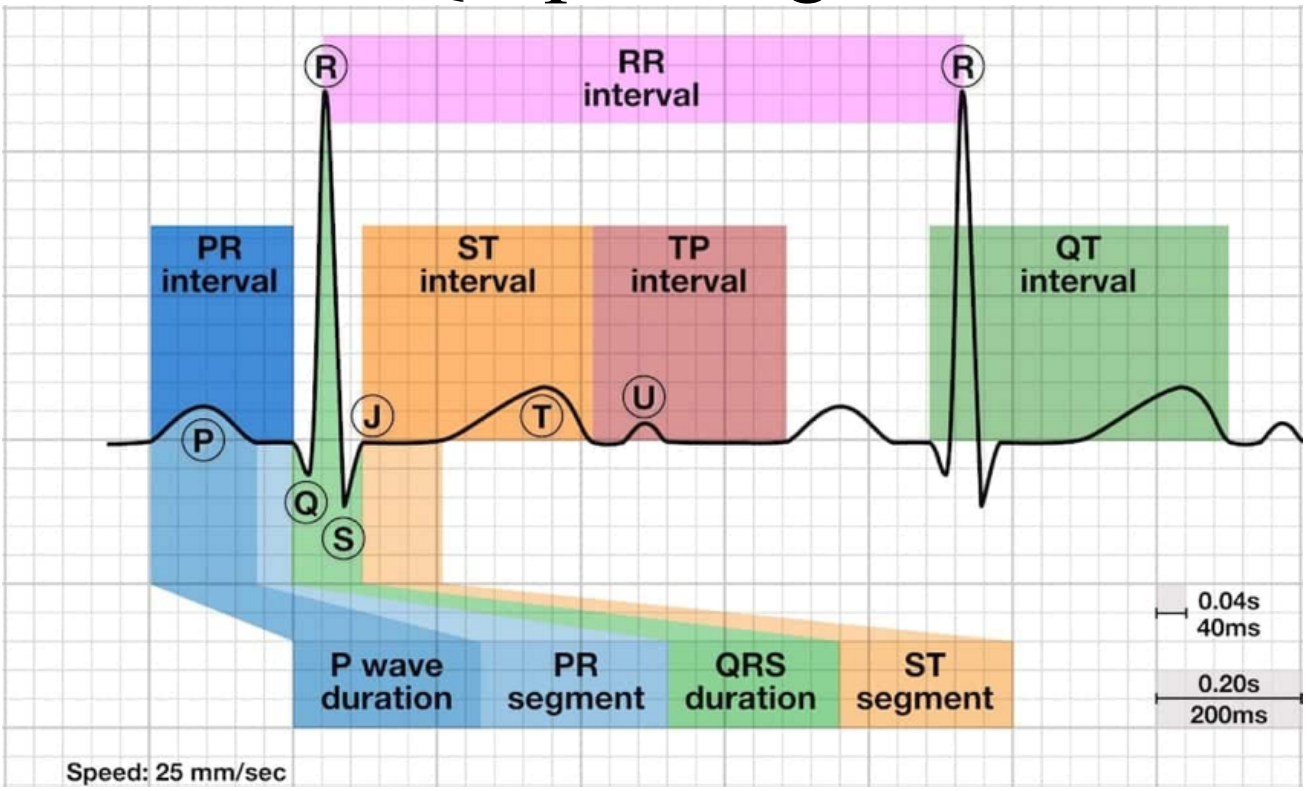
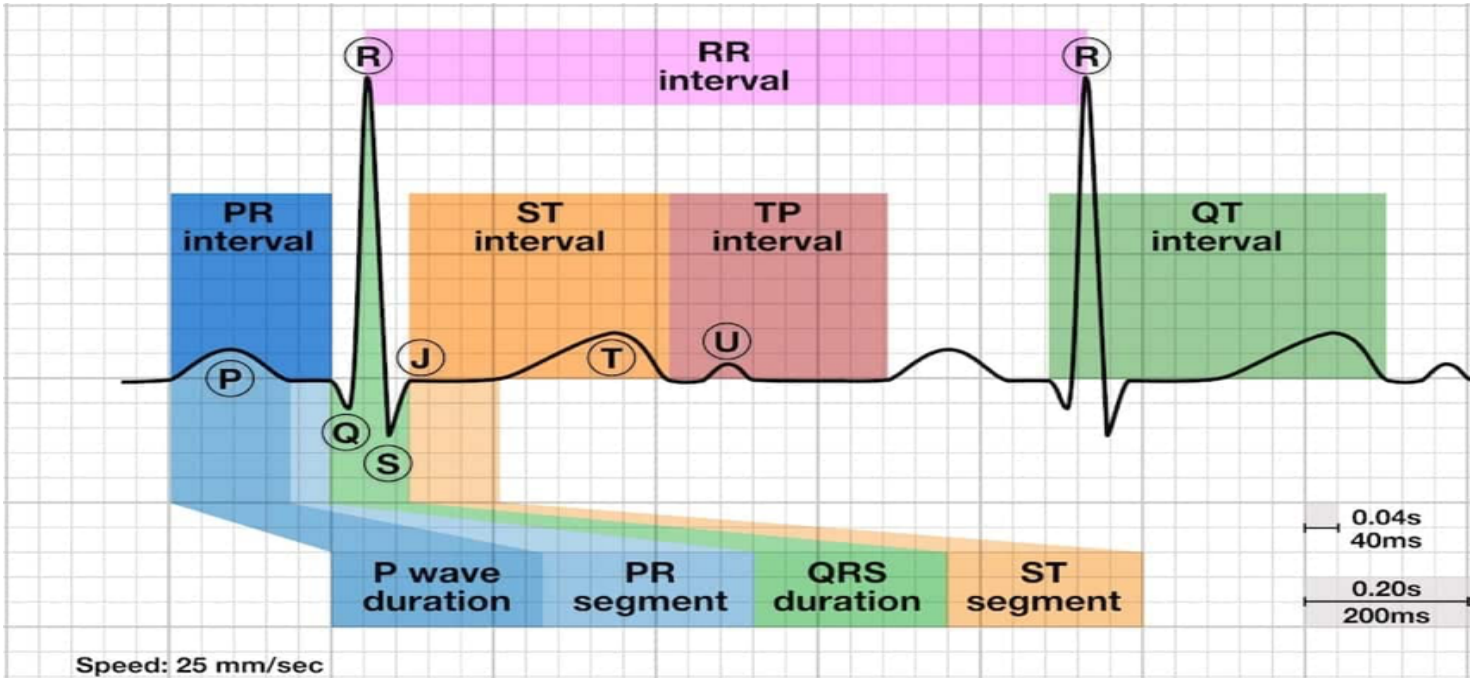
QT prolongation in Psychotropics

Mohammed Aboukaoud, PharmD, MD

What is QT prolongation?

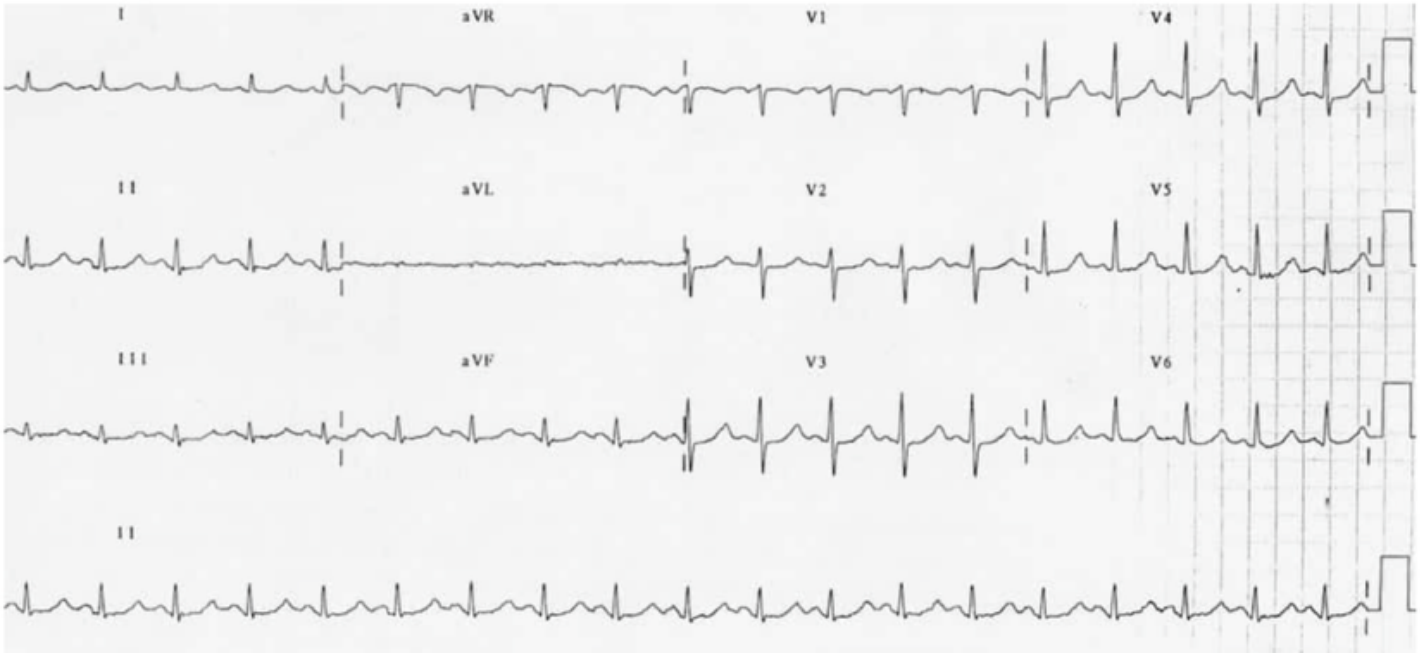


- ≥450(♂) ms
- ≥ 470(♀) ms
- ≥500ms (high risk for Tdp)



The maximum slope intercept method is used to define the end of the T wave

How do we see QT prolongation in the eye?



Better count boxes, not use QT reported by machine

90% of disagreements were ≥15 ms between machine and manual counting

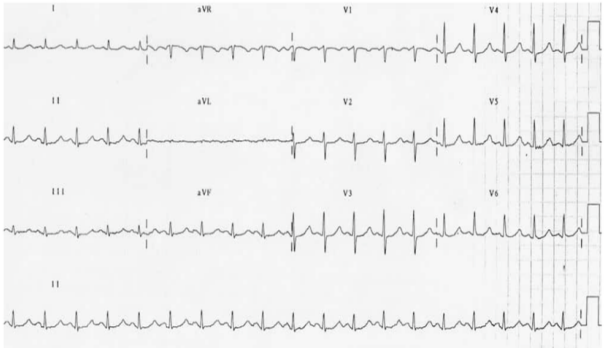
Automated readers struggle with biphasic, notched, or low-amplitude T-waves

Use Lead II first; the T-wave is usually well-defined, U-waves are usually small or absent

Lead V5 second; clean T-wave morphology, less U-wave contamination than V2–V3, and it's the standard lead for LV repolarization

Which formula to use for QTc?

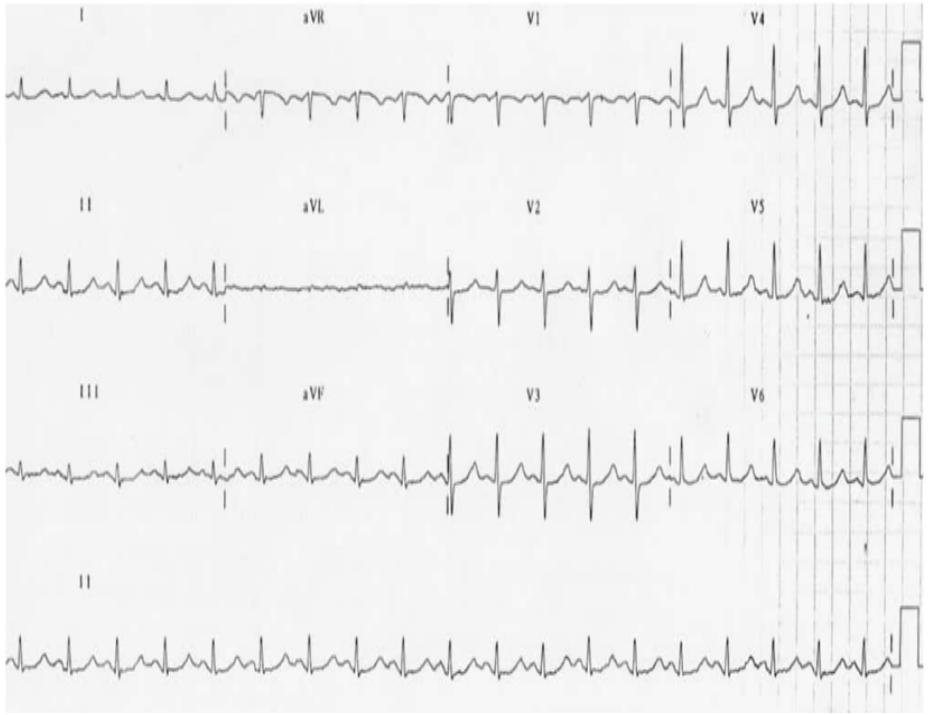
- Bazett was derived from just 39 young subjects and overcorrects at tachycardia and undercorrects at bradycardia. It performed poorly across all heart rates in a 324-ECG. Remains the default on almost every automated ECG machine.
- Framingham works well at normal rates (derived from 5,018 subjects, median age 44) but undercorrects above ~100 bpm and misbehaves at bradycardia.
- Rautaharju (derived from 57,595

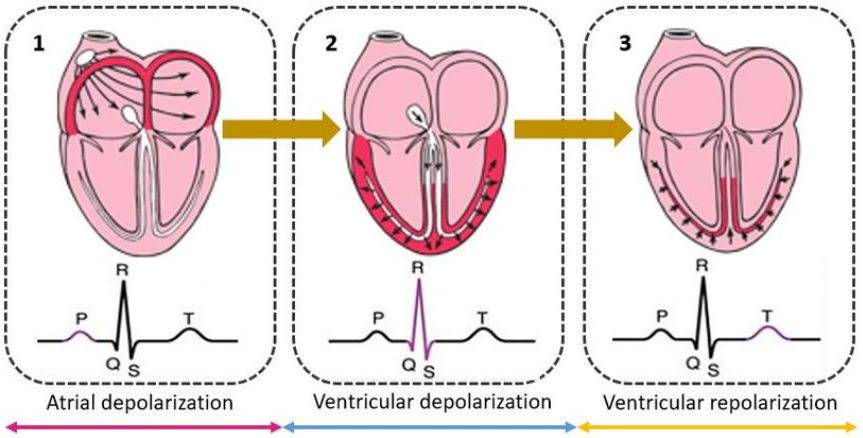


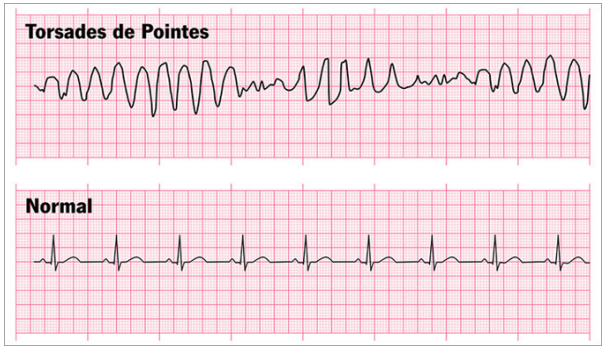
Formula	**Bazett** / **Fridericia** / **Framingham** / **Hodges** / **Rautaharju**
Heart rate/pulse	Norm: 60 - 100 beats/min
Paper speed, mm/sec	**25** / **50**
QT interval	small boxes

Toggle unit to use msec or small boxes; 1 small box = 40 msec
(see below for example where QT interval = 4 small boxes)

Pathophysiology







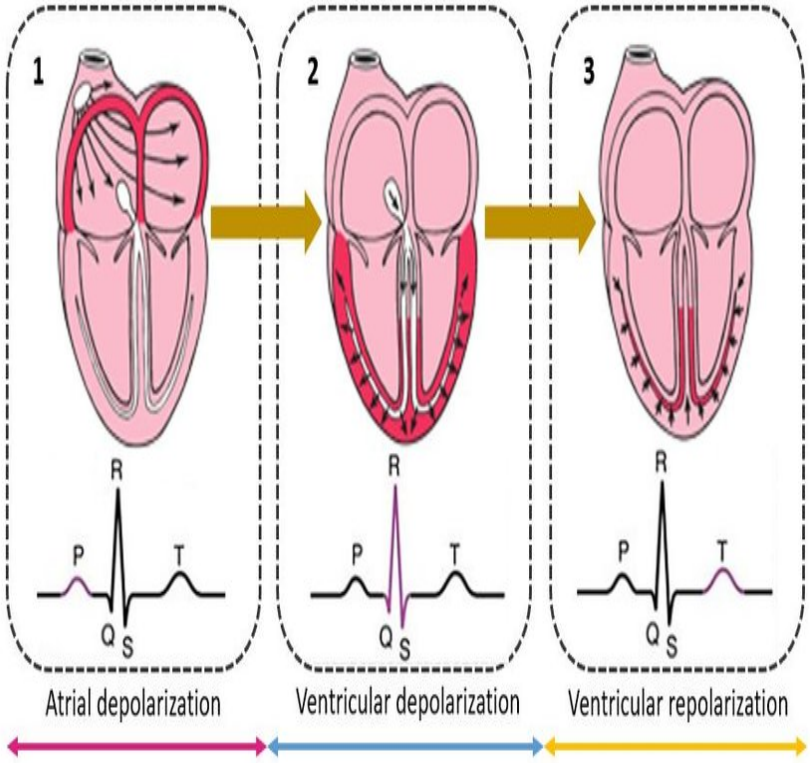
Drugs that prolong QTc

- תרופות בעלות השפעה נמוכה הן תרופות שלגביהן דווח על הארכה משמעותית של QTc מקטע לאחר מנת יתר, או כאלה שבהן נצפתה עלייה ממוצעת קטנה פחות מ-10 מילישניות במינונים טיפוליים.
- תרופות בעלות השפעה בינונית הן תרופות שנמצא כי הן מאריכות את מקטע QTc ביותר מ-10 מילישניות בממוצע כאשר הן ניתנות במינונים טיפוליים.
- תרופות בעלות השפעה גבוהה הן תרופות שלגביהן קיימת הארכה ממוצעת ניכרת של QTc קטע בדרך כלל מעל 20 מילישניות במינונים טיפוליים.

איזה מבין האנטיפסיכוטים הבאים מאריך מקטע QTc באופן משמעותי?

- Olanzapine
- Cariprazine
- IM haloperidol 5mg
- Amisulpiride
- Clozapine

Antipsychotics

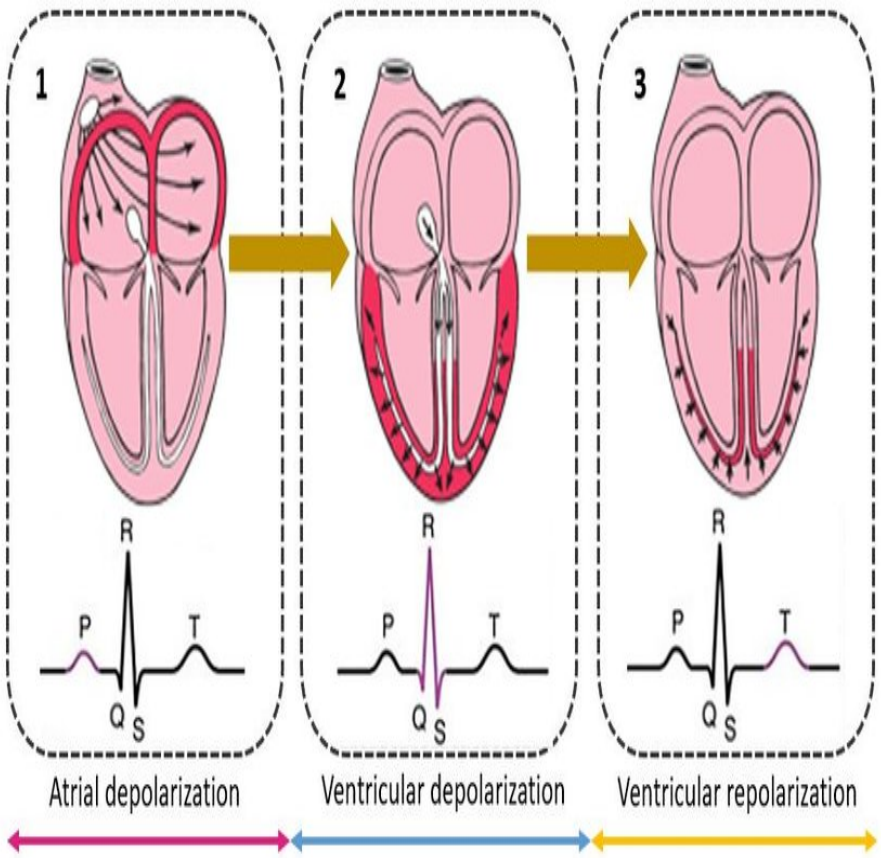


איזה מבין השילובים מומלץ לנטר אק"ג?

- Fluoxetine-aripiprazole
- Paroxetine-bupropion
- Citalopram-fluvoxamine
- Venlafaxine-mirtazapine
- Bupropion-dextromethorpan

Antidepressants QTc Prolongation

Citalopram[1,9–12] (assume same for **escitalopram**)	Small decrease in heart rate	Slight drop in systolic blood pressure	Dose-related increase in QTc	Torsade de Pointes reported, mainly in overdose
Dextromethorphan + bupropion[13]	As per bupropion	As per bupropion	As per bupropion. QTc prolongation in dextromethorphan overdose.[14]	As per bupropion
Duloxetine[1,15–17]	Slight increase	Important effect (see SPC). Caution in hypertension.	Isolated reports of QT prolongation	Isolated reports of toxicity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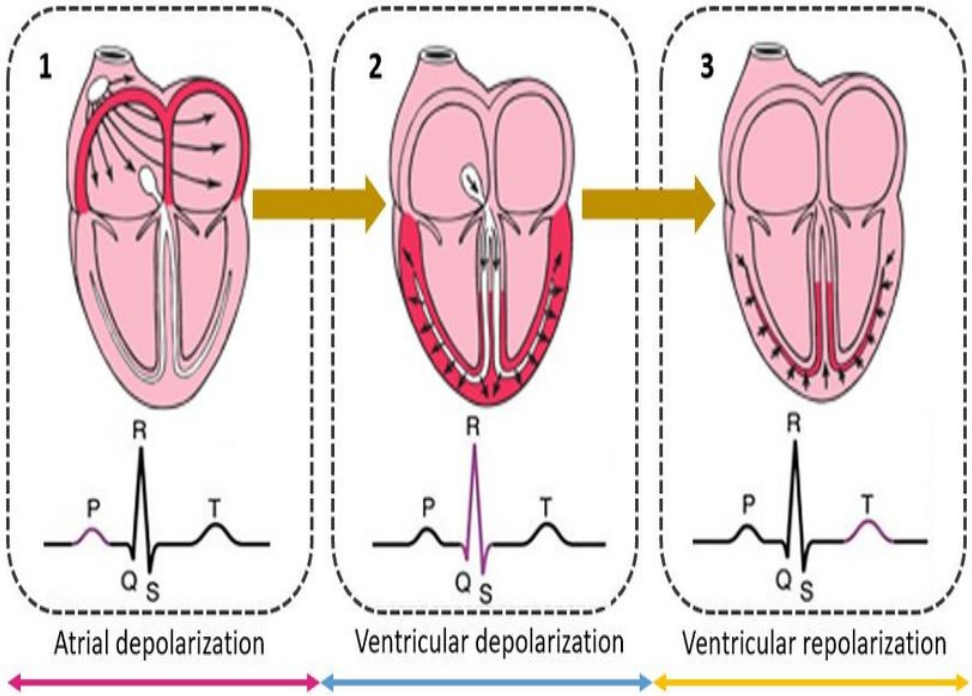
Atrial depolarization
Ventricular depolarization
Ventricular repolarization

Table 3.13 (*Continued*)

Drug	Heart rate	Blood pressure	QTc	Arrhythmia
Sertraline[12,39–42]	Minimal effect on heart rate	Minimal effect on BP	No effect on QTc interval at standard doses. Small increase (<10ms) at 400mg/day.[43]	None
Trazodone[26,44–46]	Decrease in heart rate more common, although increase can also occur	Can cause significant postural hypotension	Can prolong QTc interval	Several case reports of prolonged QT and arrhythmia
Tricyclics[26,47,48]	Increase in heart rate	Postural hypotension	Prolongation of QTc interval† and QRS interval	Ventricular arrhythmia common in overdose. Torsade de Pointes reported.
Venlafaxine[15,49–53] (assume same for **desvenlafaxine**)	Marginally increased	Some increase in postural blood pressure. At higher doses increase in BP.	Possible prolongation in overdose, but very rare	Rare reports of cardiac arrhythmia in overdose
Vilazodone[54–56]	Increased in overdose	Increased in overdose	No effect, even in overdose	No reports, even in overdose
Vortioxetine[57–59]	No effect	No effect	No effect	No effect

For more drugs use crediblemeds



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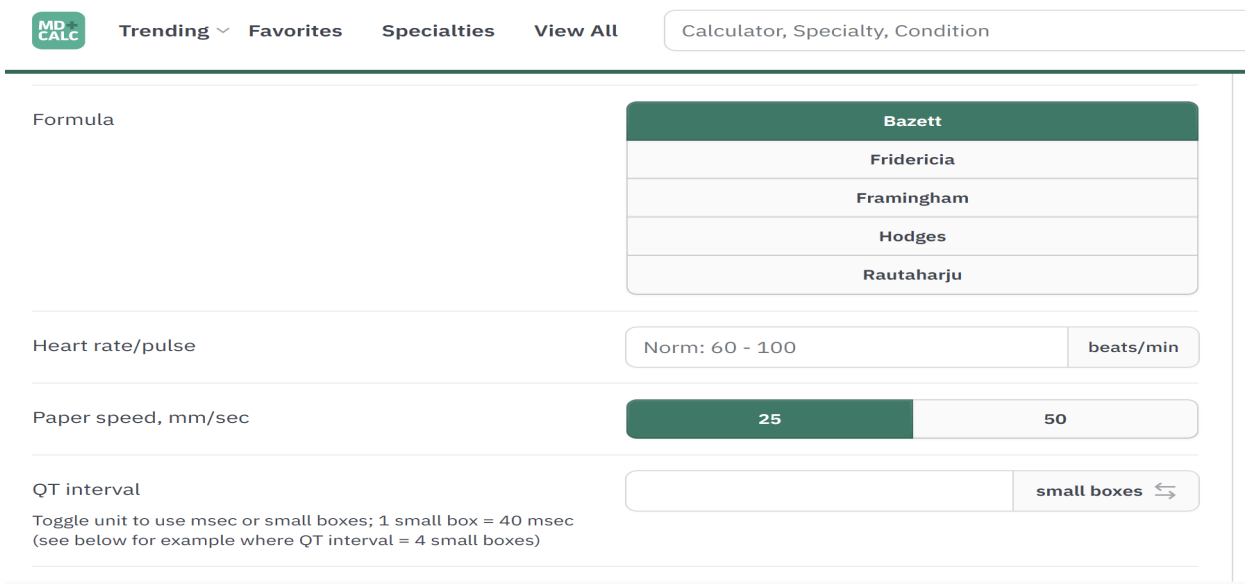
QTc? כיצד מעריכים סיכון גבוה להארכת מקטע

- להארכת מקטע high risk ו-low risk ישנם מחשבונים שונים שמקטלגים מטופלים כ כלי קליני מתוקף שנועד לזהות מטופלים QTc מדד סיכון להארכת) RISQ-PATH כתוצאה QTc מאושפזים המצויים בסיכון גבוה או נמוך לפתח הארכה של מקטע ואינם נדרשים low risk-מטיפול תרופתי. מטופלים מתחת ל-10 נקודות מוגדרים כ RISQ-PATH למעקב נוסף מעבר לאק"ג בסיס. להלן קריטריונים לחישוב ניקוד

Risk Factor	Points Allocated
Age ≥65 years	3
Female gender	3
Smoking	3
Body mass index ≥30 kg/m^2	1
Ischaemic cardiomyopathy	3
Hypertension	3
Arrhythmia	3
Prolonged QT interval on baseline ECG	6
Thyroid disturbance	3
Liver failure	1
Neurological disorder (stroke, trauma, infection, tumour)	0.5
Diabetes	0.5
Hypokalaemia (potassium ≤3.5 mmol/L)	6
Hypocalcaemia (calcium <2.15 mmol/L)	3
CRP >5mg/L (inflammation)	1
Renal impairment (eGFR ≤30 mL/min/1.73 m^2)	0.5
For each known risk category 1 drug	3
For each possible risk category 2 drug	0.5
For each conditional risk category 3 drug	0.25
Total RISQ-PATH score	Max 40.5 + sum QT drugs

CRP, C-reactive protein; ECG, electrocardiogram.

מה עושים כאשר יש הארכה במקטע QTc?



Differences in Ventricular Tachyarrhythmia and Sudden Cardiac Death Reporting Among Antipsychotics: A VigiBase Analysis

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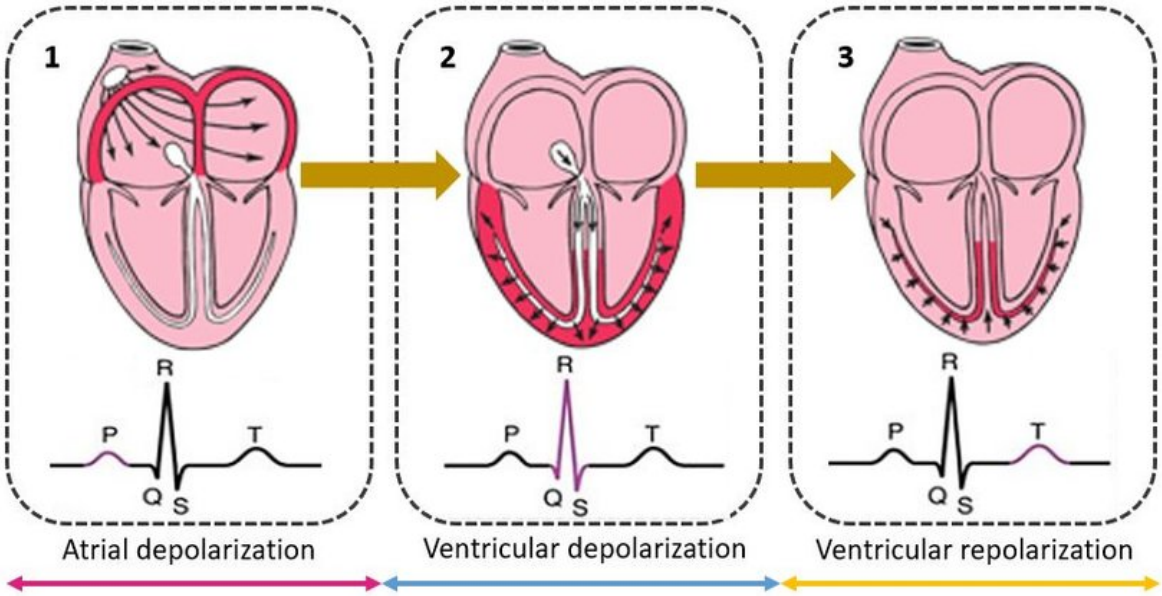
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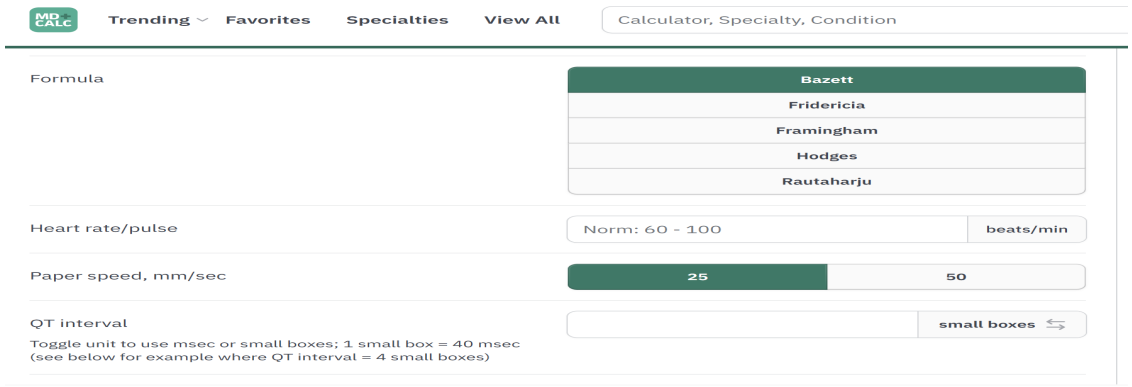
Ventricular depolarization
Ventricular repolarization



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