

# EVERYTHING THE PSYCHIATRIST NEEDS TO KNOW ABOUT ECGs

Margo Funk, MD, MA, FACLP      May 5, 2024

## **Margo C. Funk, MD, MA**

With respect to the following presentation, there has been no relevant (direct or indirect) financial relationship between the party listed above (and/or spouse/partner) and any for-profit company which could be considered a conflict of interest.

# ACKNOWLEDGEMENTS

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**Scott R. Beach, MD**



**Chris Celano, MD**

## APA OFFICIAL ACTIONS

### APA Resource Document on QTc Prolongation and Psychotropic Medications

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# CASE 1

27 y/o woman with history of GAD and social phobia, well controlled on citalopram 40mg po daily, presents to your outpatient clinic to establish care after relocating for her first job out of law school.

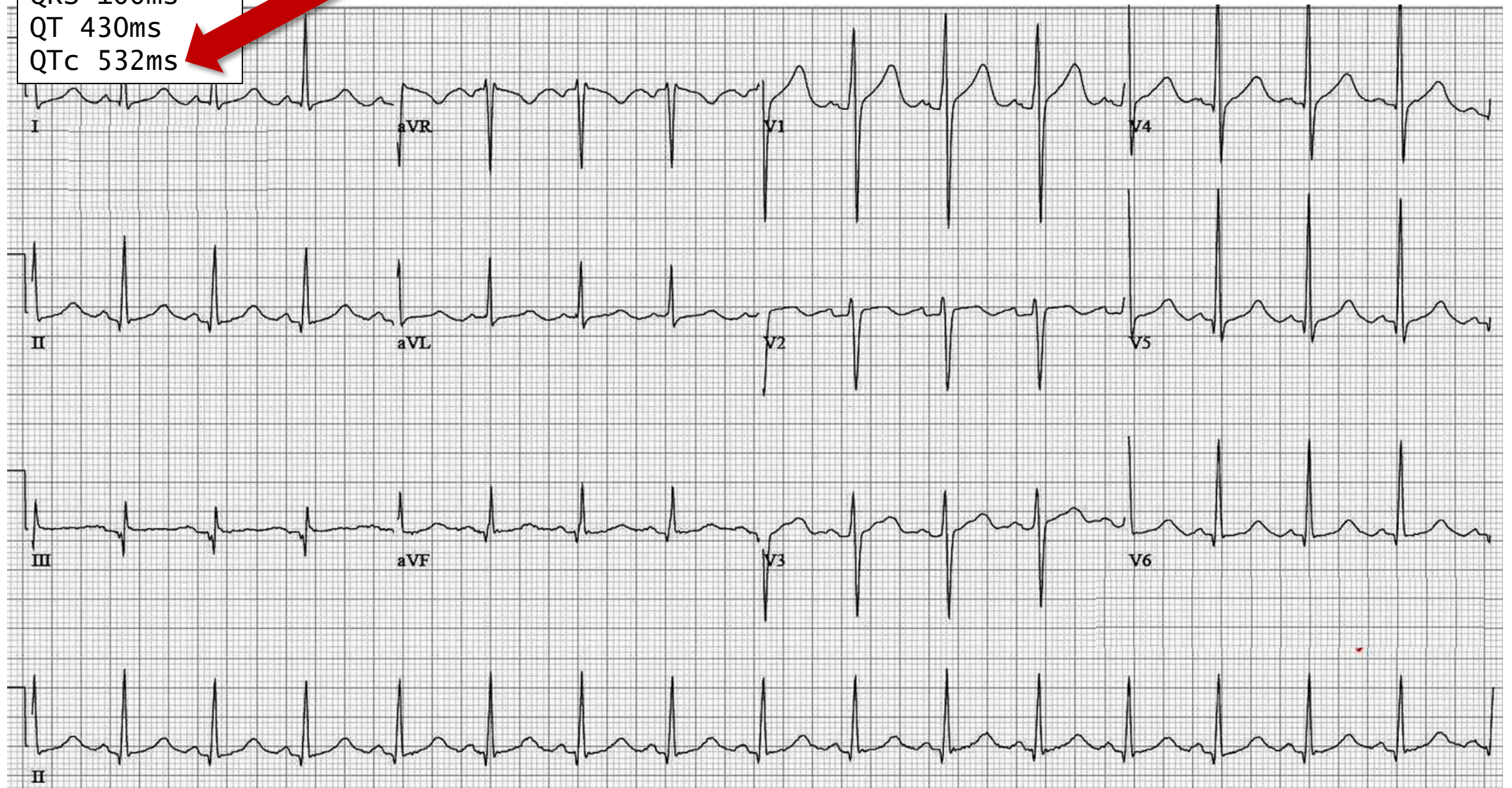
She has no significant past medical history, takes no other medications, has no family history of arrhythmia, cardiac arrest or sudden death. She has no suicide attempts, no inpatient psychiatric hospitalizations.

Your clinic just purchased an ECG machine, and the medical assistants were recently trained how to use the machine. While you believe her cardiac risk factors to be very low, since you have the resource available, you decide to obtain an ECG for the sake of completeness.



HR 92 bpm  
QRS 100ms  
QT 430ms  
QTc 532ms

!!!???



# OBJECTIVES

- Describe indications for obtaining an ECG when initiating psychiatric medications with elevated cardiac risk
- Correlate ECG waves and intervals, including the QT interval, QRS complex, and T wave, to the underlying electrophysiologic processes.
- Accurately measure the QT interval and calculate the QTc using an appropriate formula
- Describe an approach to risk-benefit assessment of starting a QTc-prolonging medication in a patient with risk factors for Torsades de Pointes.



# COMPUTER-DERIVED ELECTROCARDIOGRAM

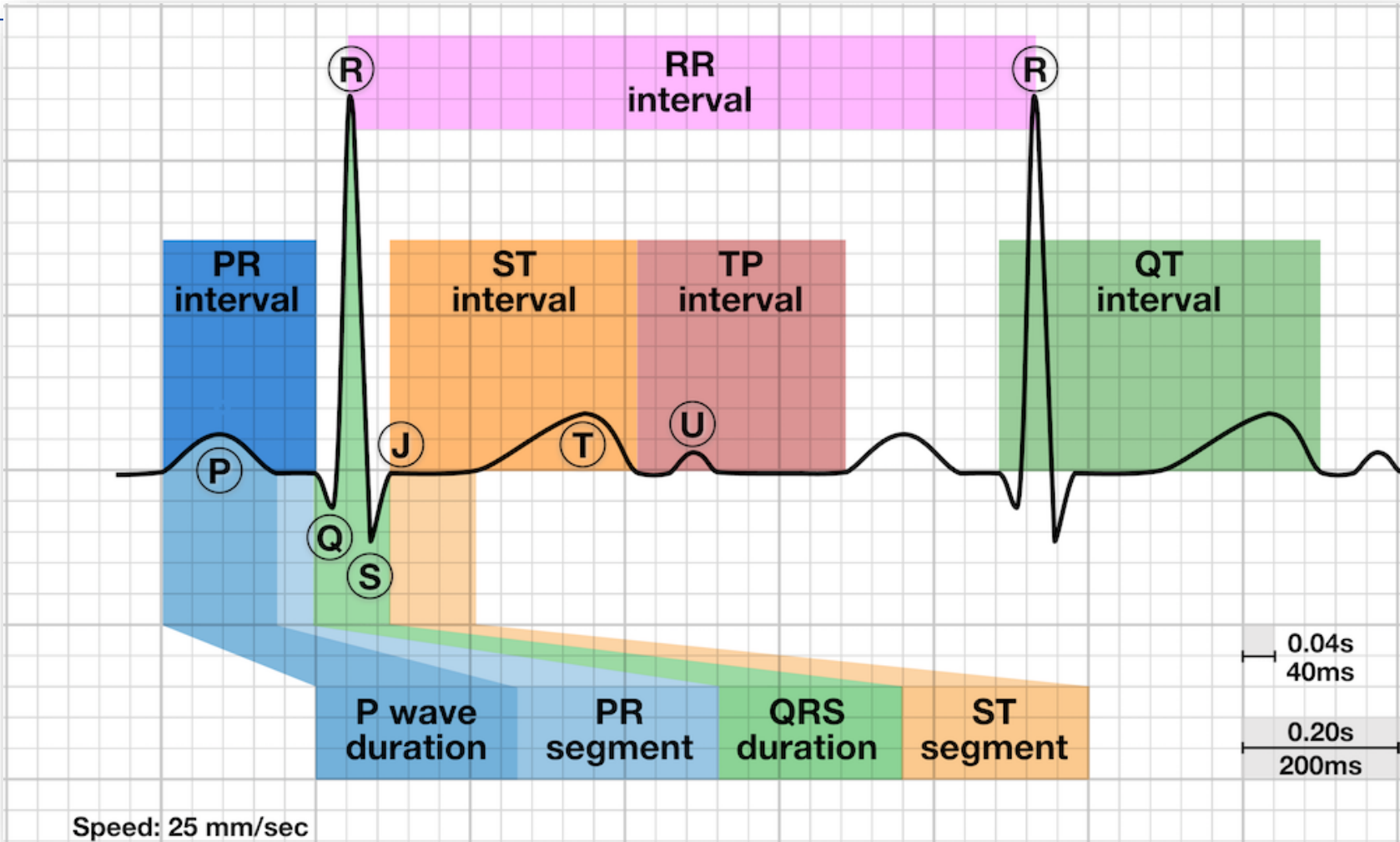
- Results differ from machine to machine
- Often are derived from “representative” or “median” complexes
- Correction method generally is the Bazett correction

**Should always be measured and interpreted by a person!**





# ECG INTERVALS



Interval	Duration (ms)
PR	120-200
QRS	80-100
ST	80
RR	600-1000

# MEASURING HEART RATE



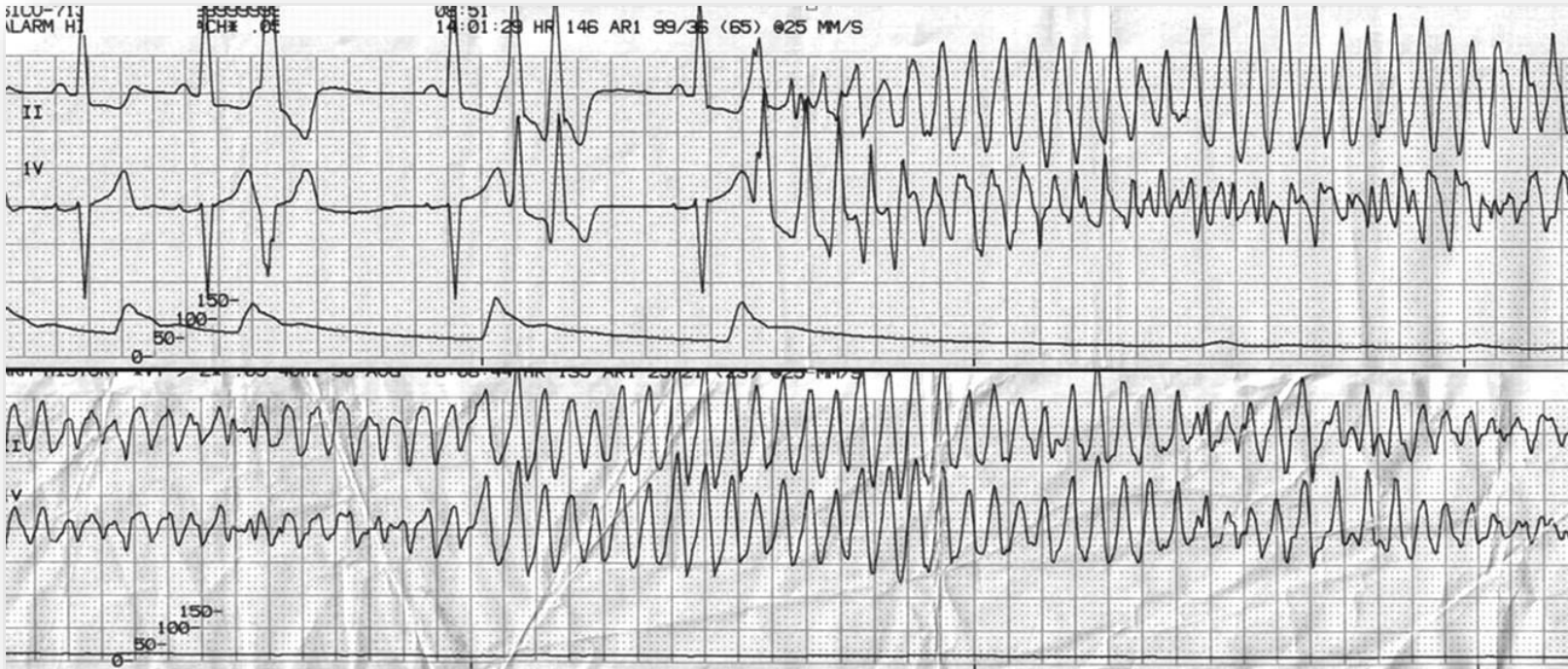
1. 12 lead ECG = 10 seconds
2. Count the number of beats
3. Multiply number of beats x 6 = Beats per minute

$$12 \text{ Beats} \times 6 = 72 \text{ bpm}$$

# THE CORRECTED QT INTERVAL (QT<sub>c</sub>)

# TORSADES DE POINTES (TDP)

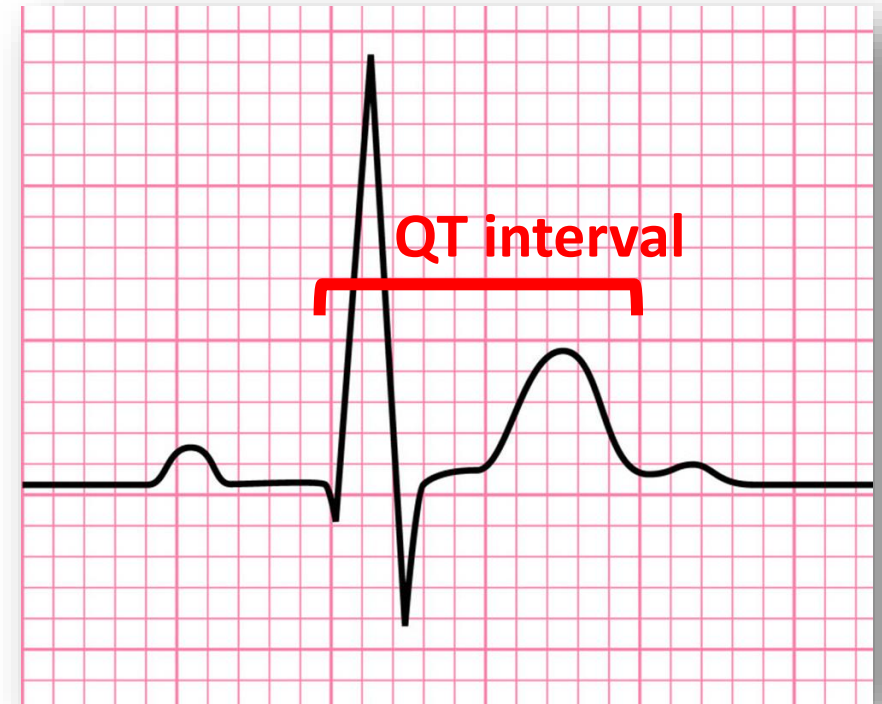
## “Twisting of the Pointes”



- a malignant polymorphic ventricular tachycardia
- lightheadedness, syncope, seizure-like activity, sudden cardiac death
- often an out-of-hospital event; difficult to study

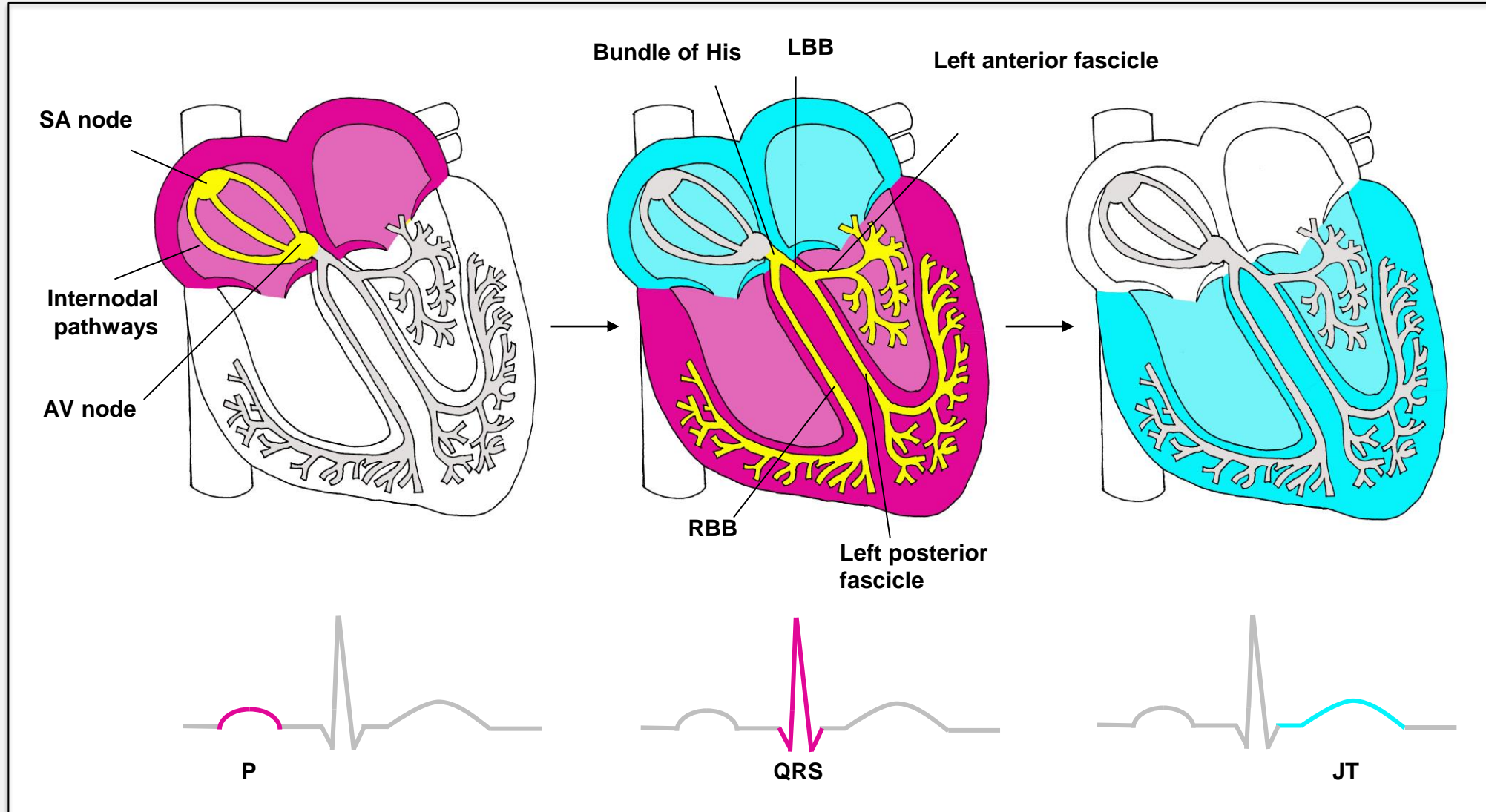
# TORSADES DE POINTES (TDP) AND QTC

- Occurs in setting of congenital vs. acquired long QT syndrome
  - congenital: genetic syndromes w/characteristic QT morphology & sudden cardiac death
  - acquired: QT prolongation occurs **under certain clinical conditions**, leading to TdP
- QTc prolongation is best marker of risk





# ELECTROPHYSIOLOGY AND THE ELECTROCARDIOGRAM

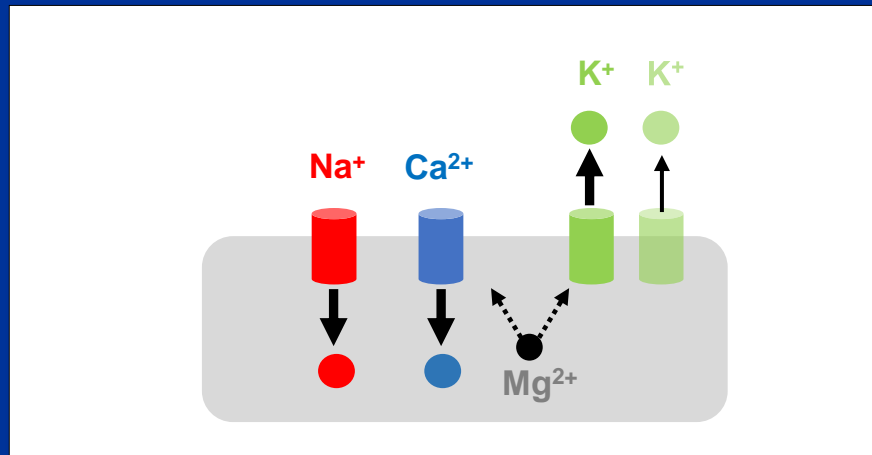
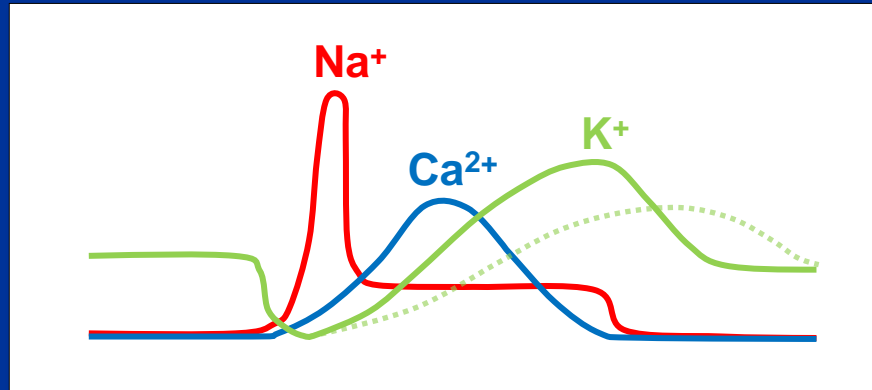


■ Depolarization ■ Repolarization

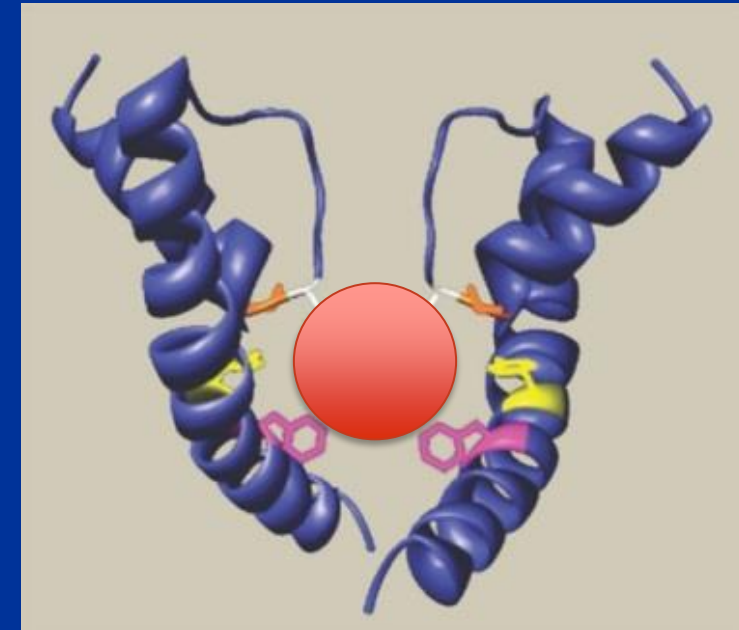
Funk et al. 2021

# PROLONGED REPOLARIZATION

## Cardiac Myocyte Action Potential



## I<sub>kr</sub> channel – HERG (human ether-a-go-go related gene)



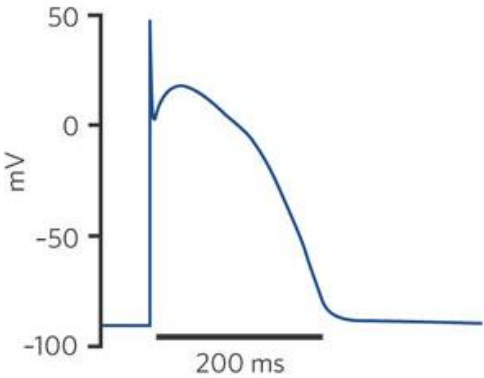
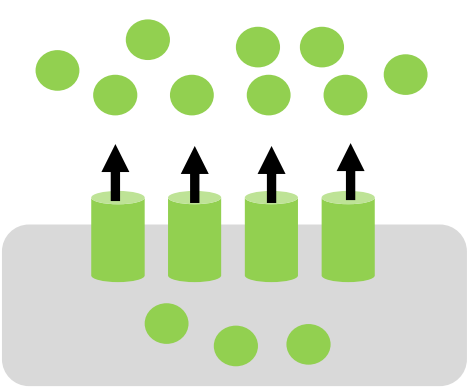
# PROLONGED REPOLARIZATION

K<sup>+</sup> Efflux

Action  
Potential

ECG

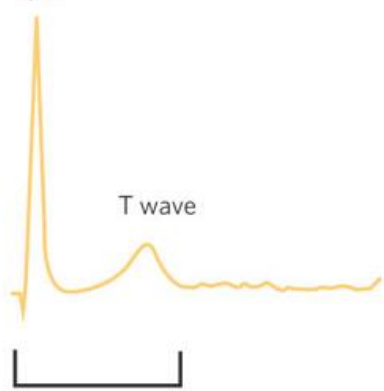
NORMAL



QRS

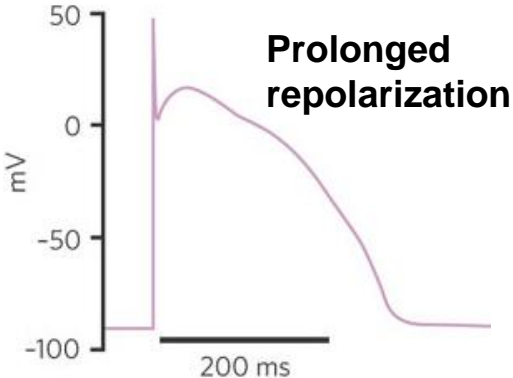
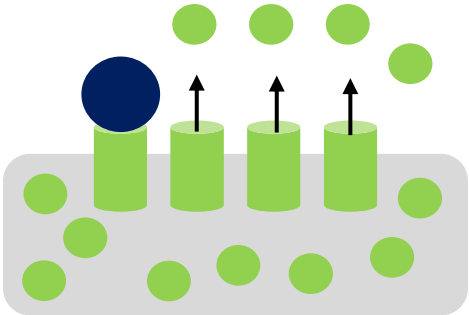
T wave

QT

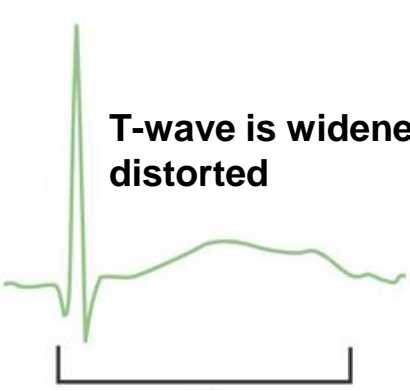


PROLONGED

hERG-blocking drug

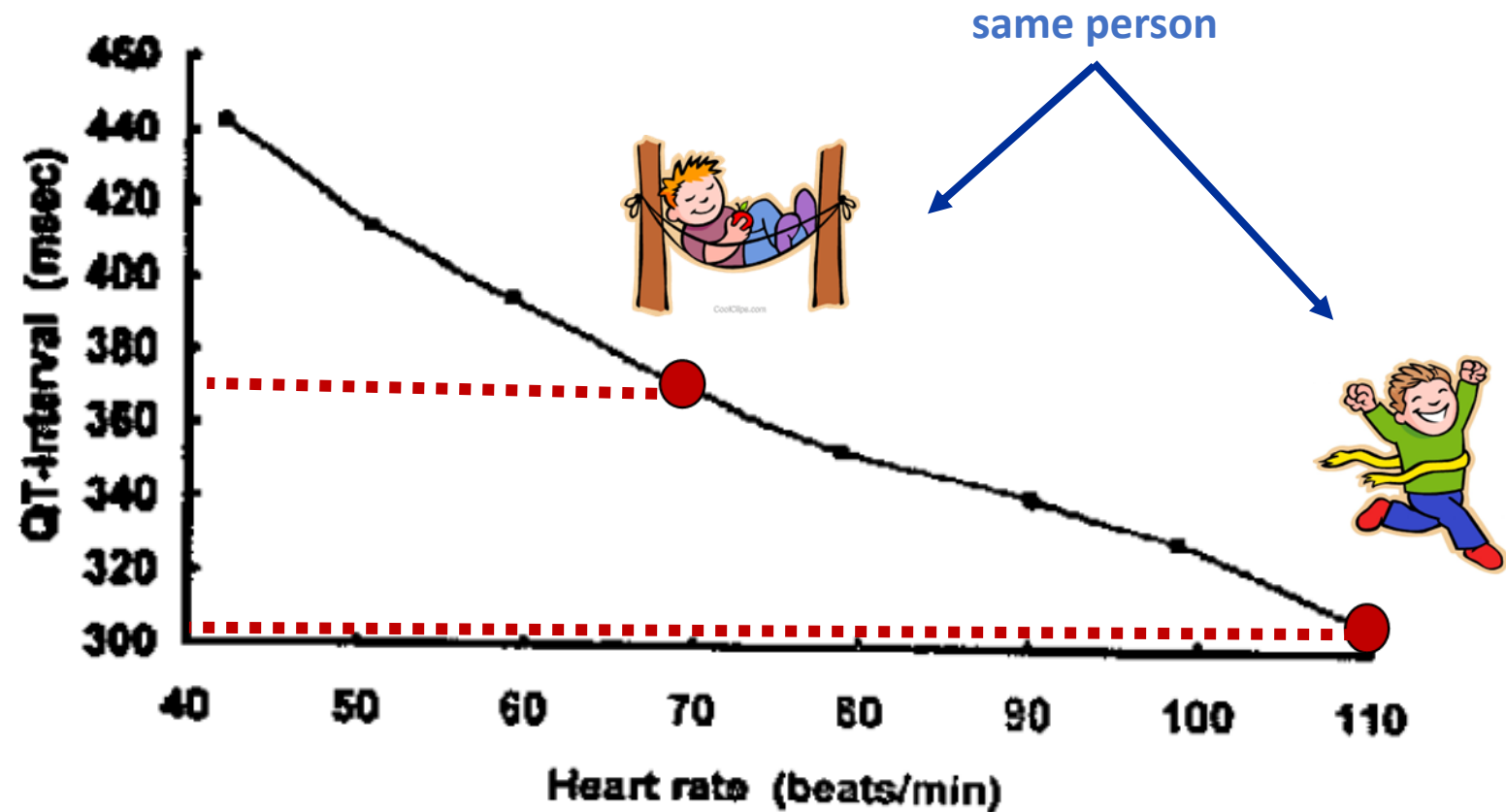


T-wave is widened,  
distorted

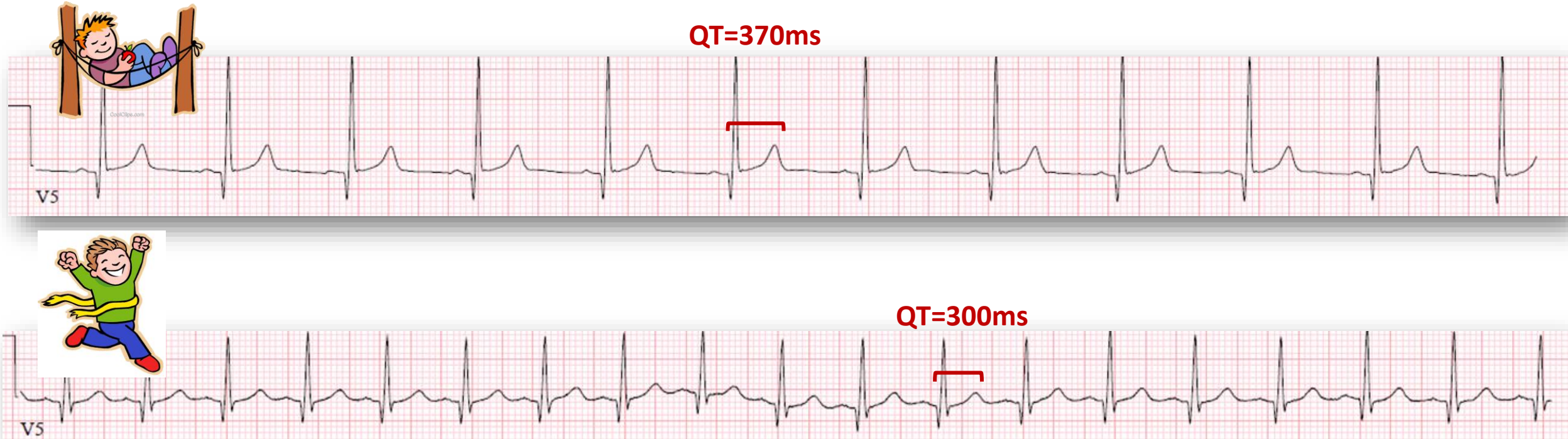


# QT INTERVAL IS HR DEPENDENT

- Absolute QT interval varies depending on HR
- The slower the heart rate, the longer the cycle length (duration of one beat), the longer the measured QT



# QT INTERVAL IS HR DEPENDENT



- Ventricular repolarization abnormalities do not change across HR in the same person
- We must correct the QT interval so we have a **consistent marker of risk** across all HR



# QTC CORRECTION FORMULAE

Method	Formula
Bazett	$QTc = QT / \sqrt{RR}$
Fridericia*	$QTc = QT / \sqrt[3]{RR}$
Framingham†*	$QTc = QT + 0.154 (1000 - RR)$
Hodges†	$QTc = QT + 1.75(HR - 60)$

† Rautaharju et al. 2009. AHA/ACC/HRS Guidelines. Recommends linear regression

\*Vandenburk et al. 2016. JAHA. Recommends Fridericia or Framingham

# QTC NORMAL RANGES

Rating	Adult Men	Adult Women
Normal	< 430 msec	< 450 msec
Borderline	431-470 msec	451-480 msec
Prolonged	> 470 msec	> 480 msec

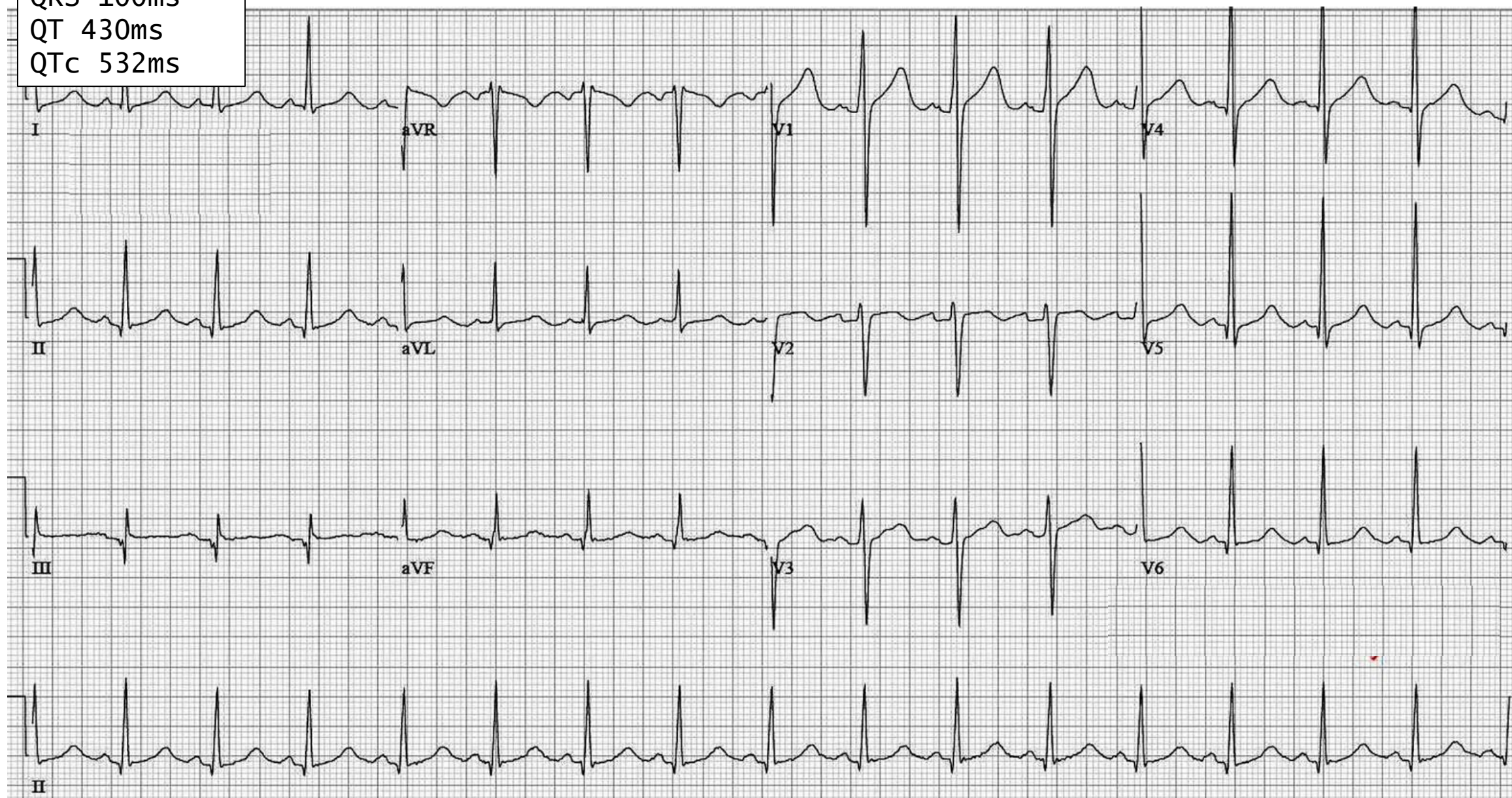
However, we generally become more concerned if:

- QTc > 500 msec
- QTc increases by  $\geq 60$  msec after medication change

\*There is not an absolute QTc at which an at-risk medication cannot be prescribed

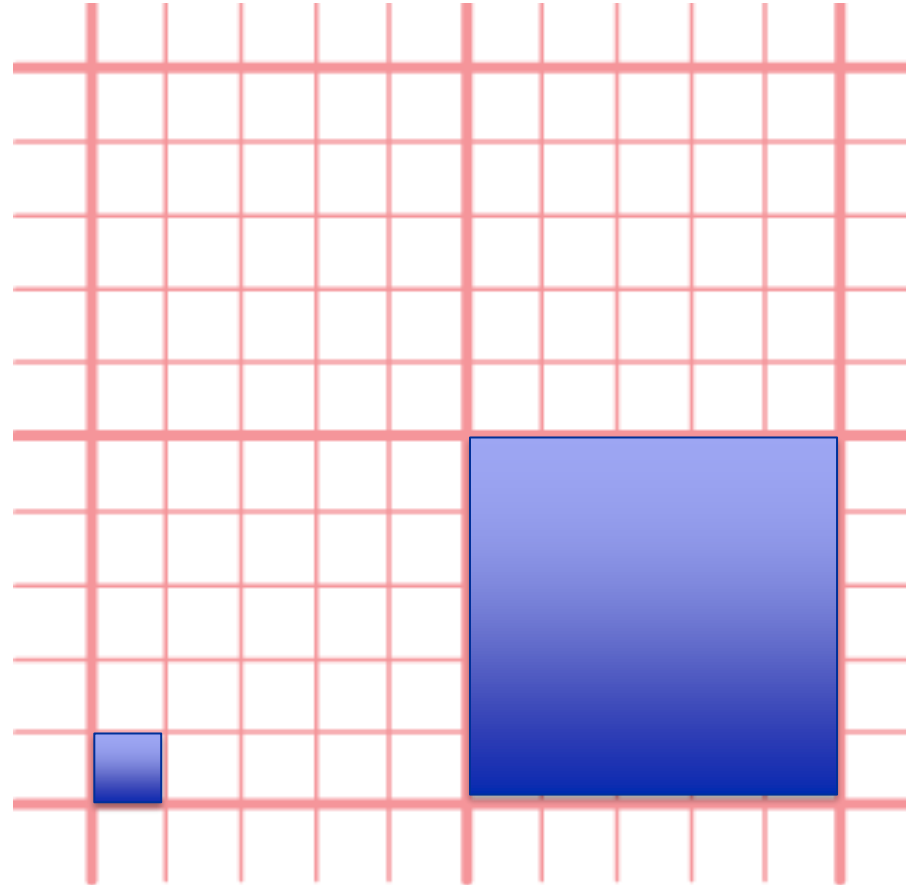
HR 92 bpm  
QRS 100ms  
QT 430ms  
QTc 532ms

## CASE 1



# MAKING YOUR OWN MEASUREMENTS & CALCULATIONS





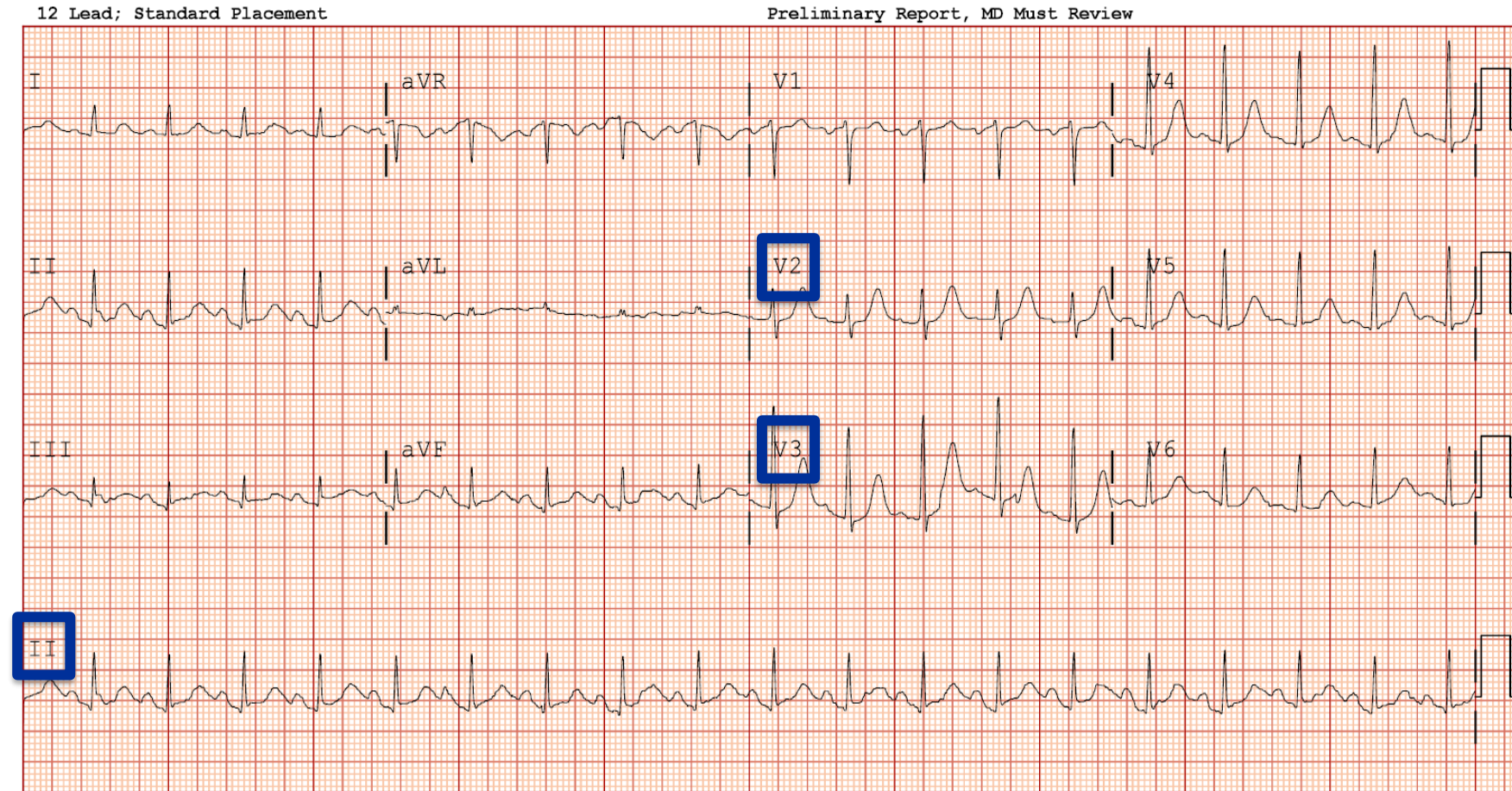
**small box = 40 msec**      **large box = 200 msec**



# MEASURING THE QT-INTERVAL

## Which Lead to Use?

- lead V2, V3 or II *or*
- lead where end of T-wave is easiest to discern *or*
- lead showing the longest QT



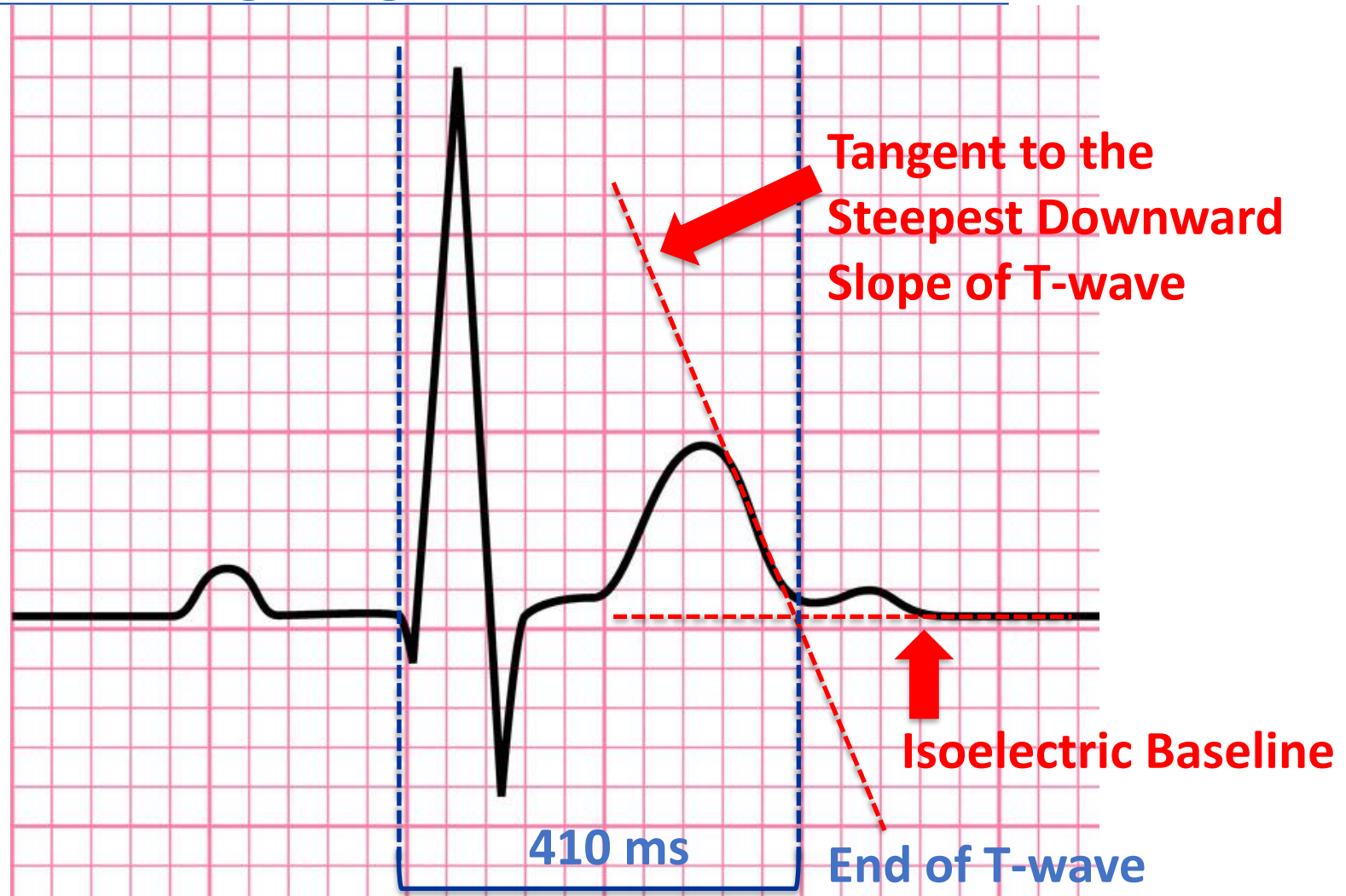
## Tangent Method

- Intersection of tangent to steepest downward slope of T-wave with isoelectric baseline



# TANGENT METHOD

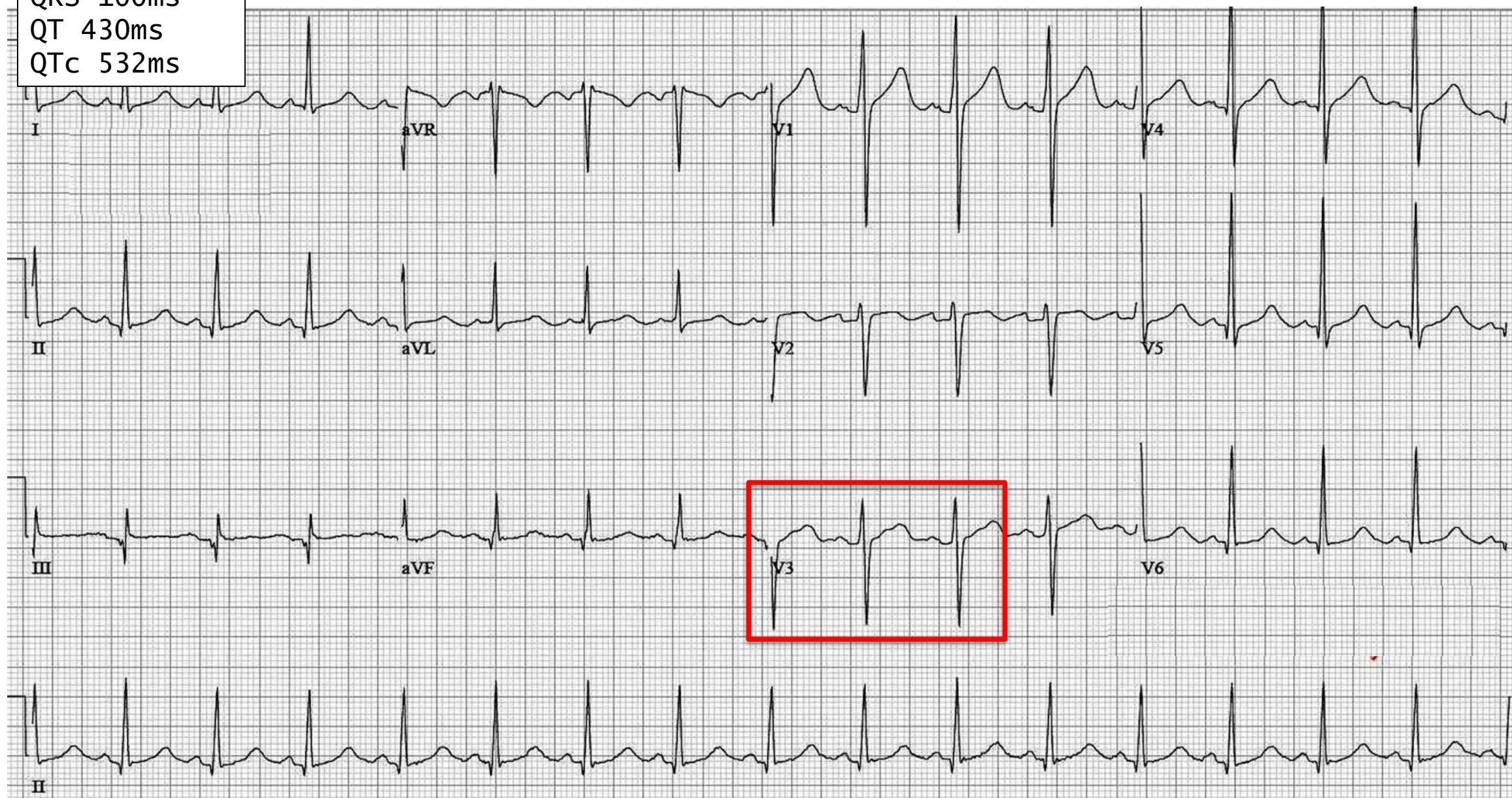
## Beginning of Q-wave





HR 92 bpm  
QRS 100ms  
QT 430ms  
QTc 532ms

## CASE 1





HR 92 bpm  
QRS 100ms  
QT 430ms  
QTc 532ms

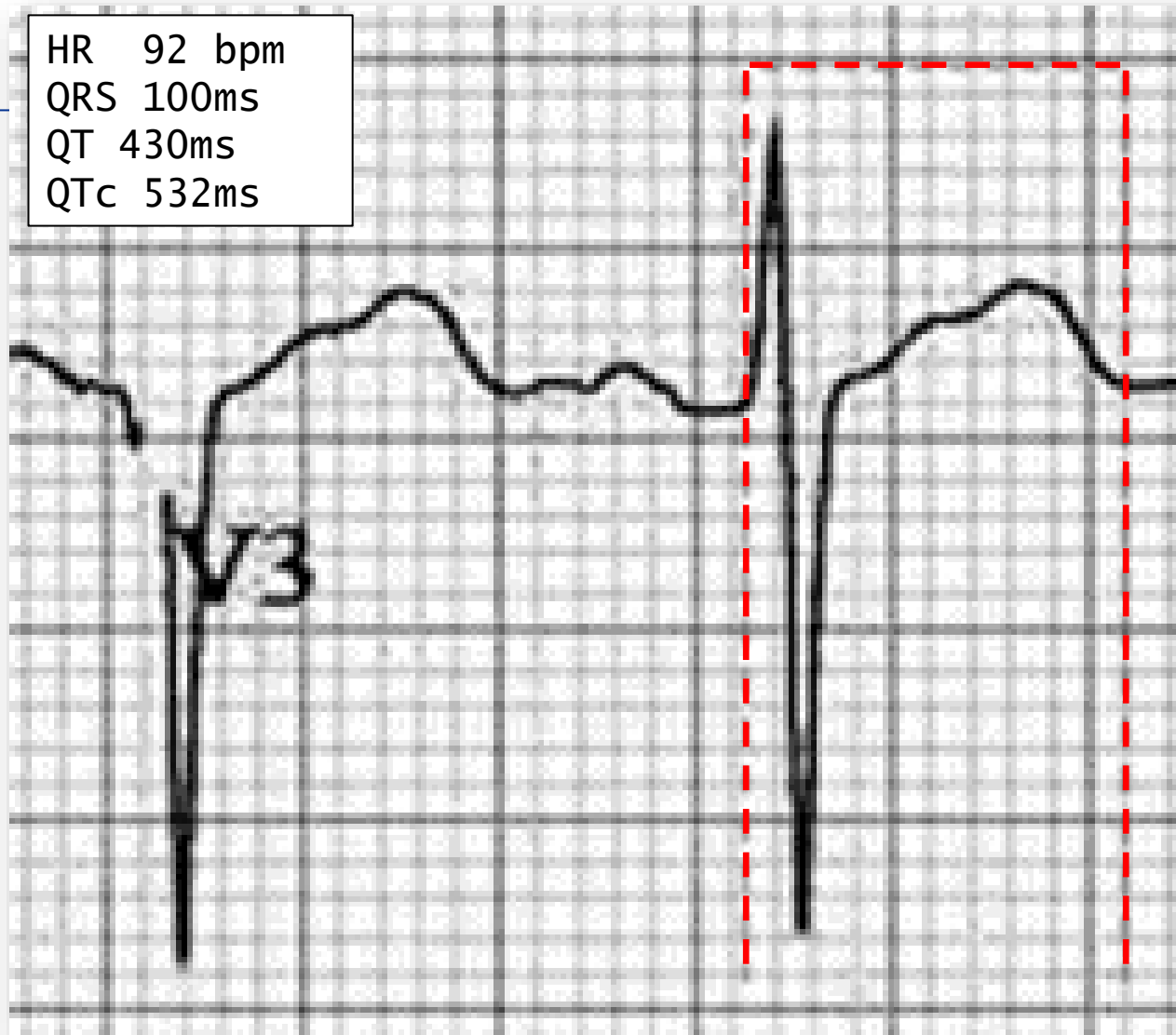
**QT = 9 boxes + 30ms = 390ms**





QT = 390 ms

HR 92 bpm  
QRS 100ms  
QT 430ms  
QTc 532ms



mdcalc.com

**MD+CALC** Search "QT interv" ☰

**Corrected QT Interval (QTc)** ☆

Corrects the QT interval for heart rate extremes (choose from Bazett, Fridericia, Framingham, Hodges, or Rautaharju formulas).

When to Use ▼ Why Use ▼

Formula

Bazett
Fridericia
Framingham
<b>Hodges</b>
Rautaharju

Heart rate/pulse 92 beats/min

Paper speed, mm/sec 25 50

QT interval Toggle unit to use msec or 390 msec ↕

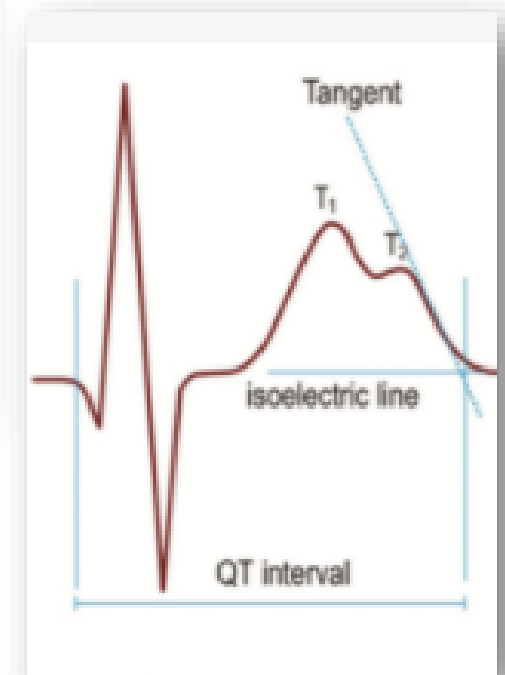
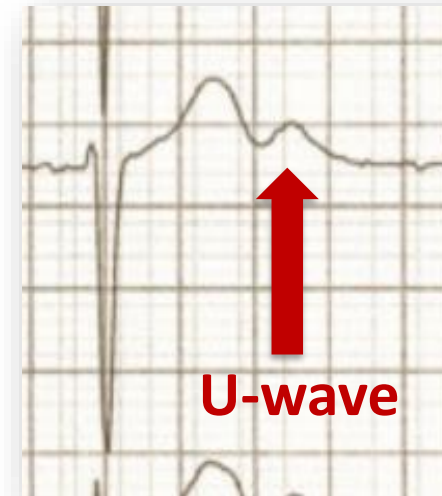
**446 msec**

QTc (B) = 483 ms  
QTc (H) = 446 ms  
QTc (Fri) = 450 ms  
QTc (Fra) = 444 ms

# WHAT ABOUT U-WAVES?

## ACC/AHA/HRS recommendation for U-waves superimposed on T-waves:

- If U-wave  $< 1/3$  amplitude of T-wave either:
  - the QT should be measured in a lead without a U wave OR
  - use tangent method to steepest downward slope of T-wave
- If U-wave  $> 1/3$  amplitude of T-wave, it is likely pathologic and should be included



# RISK ASSESSMENT AND MEDICATIONS

# RISK FACTORS FOR TDP

Non-modifiable risk factors	Modifiable risk factors
<ul style="list-style-type: none"><li>● Female sex</li><li>● Advanced age</li><li>● Metabolizer status</li><li>● Congenital long QT syndrome</li><li>● Personal history of drug-induced QTc prolongation</li><li>● Personal history of structural or functional cardiac disease</li><li>● Family history of sudden cardiac death</li></ul>	<ul style="list-style-type: none"><li>● Use of <math>\geq 1</math> QTc prolonging drug(s)</li><li>● Pharmacokinetic drug-drug interactions</li><li>● Drug toxicity</li><li>● Severe acute illness</li><li>● Bradycardia</li><li>● Starvation</li><li>● Hepatic impairment</li><li>● Renal impairment, hemodialysis</li><li>● Risk or presence of hypokalemia, hypomagnesemia or hypocalcemia</li></ul>

# MEDICATIONS AND RISK OF TDP



QTc prolongation is a major drug safety benchmark used by FDA and other international regulatory agencies



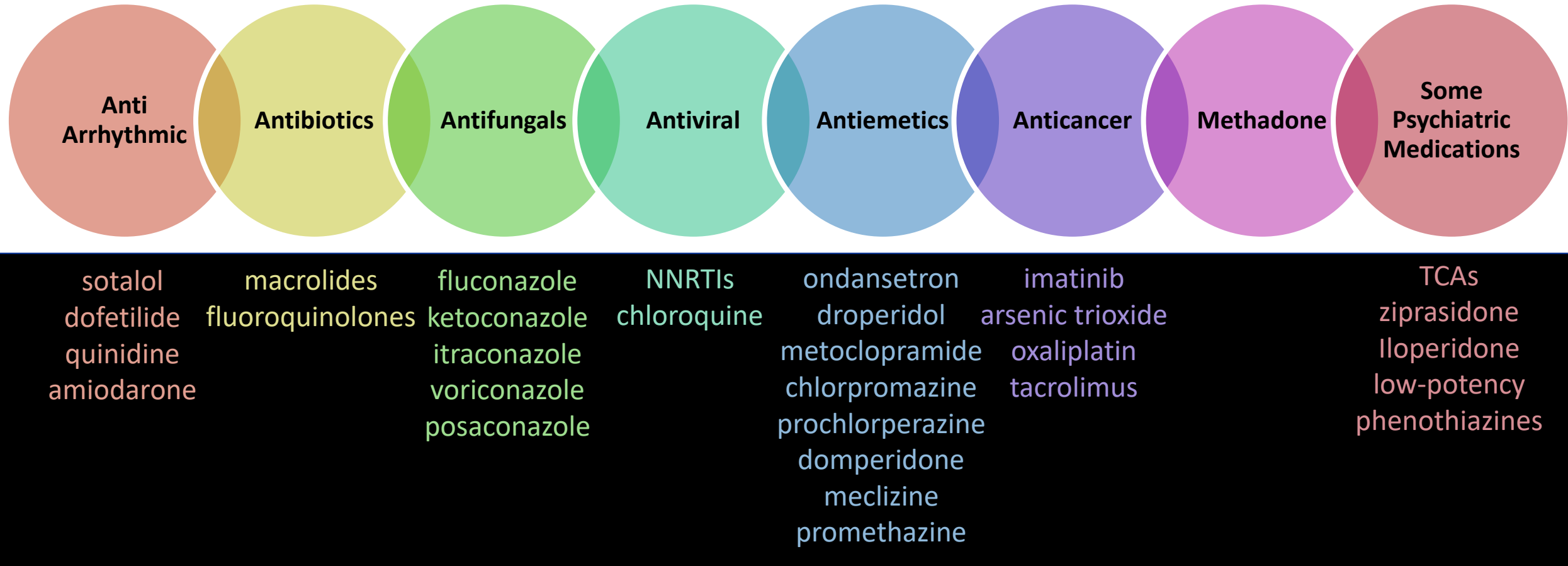
QTc prolongation is only a marker of risk for TdP



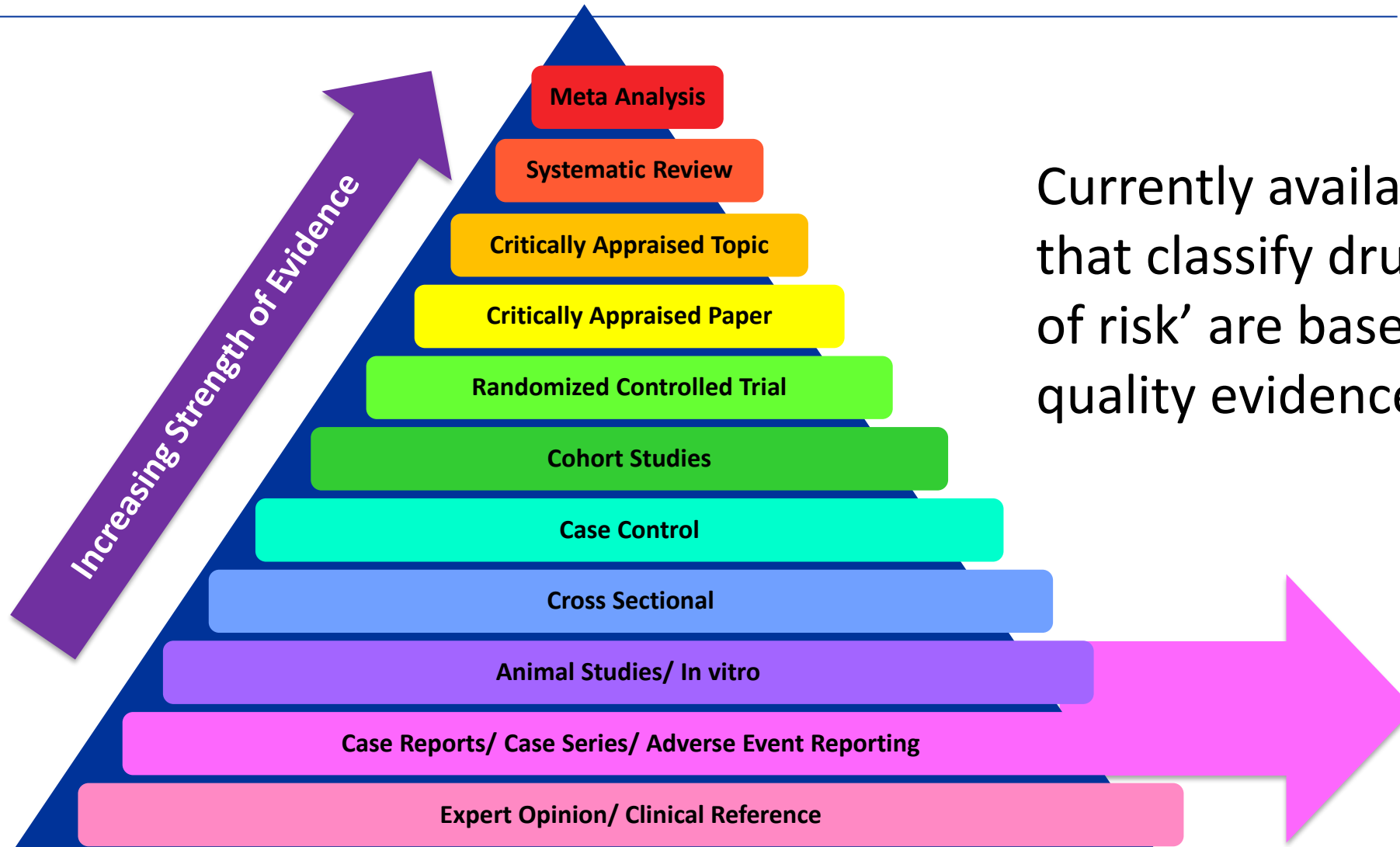
In the absence of other risk factors, drug-induced QTc prolongation rarely leads to TdP



# MEDICATIONS ASSOCIATED WITH PROLONGED QTC & TDP



# LIMITATIONS OF AVAILABLE DATA



Currently available drug registries that classify drugs according to ‘level of risk’ are based mostly on lower quality evidence

**QTc and Torsades Risk Drug Registries**

# LIMITATIONS OF AVAILABLE DATA

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Study population

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Method of QTc measurement and correction

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Timing of measurement

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Medication dose

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Concomitant medications

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Reported QTc prolongation: clinically meaningful change?

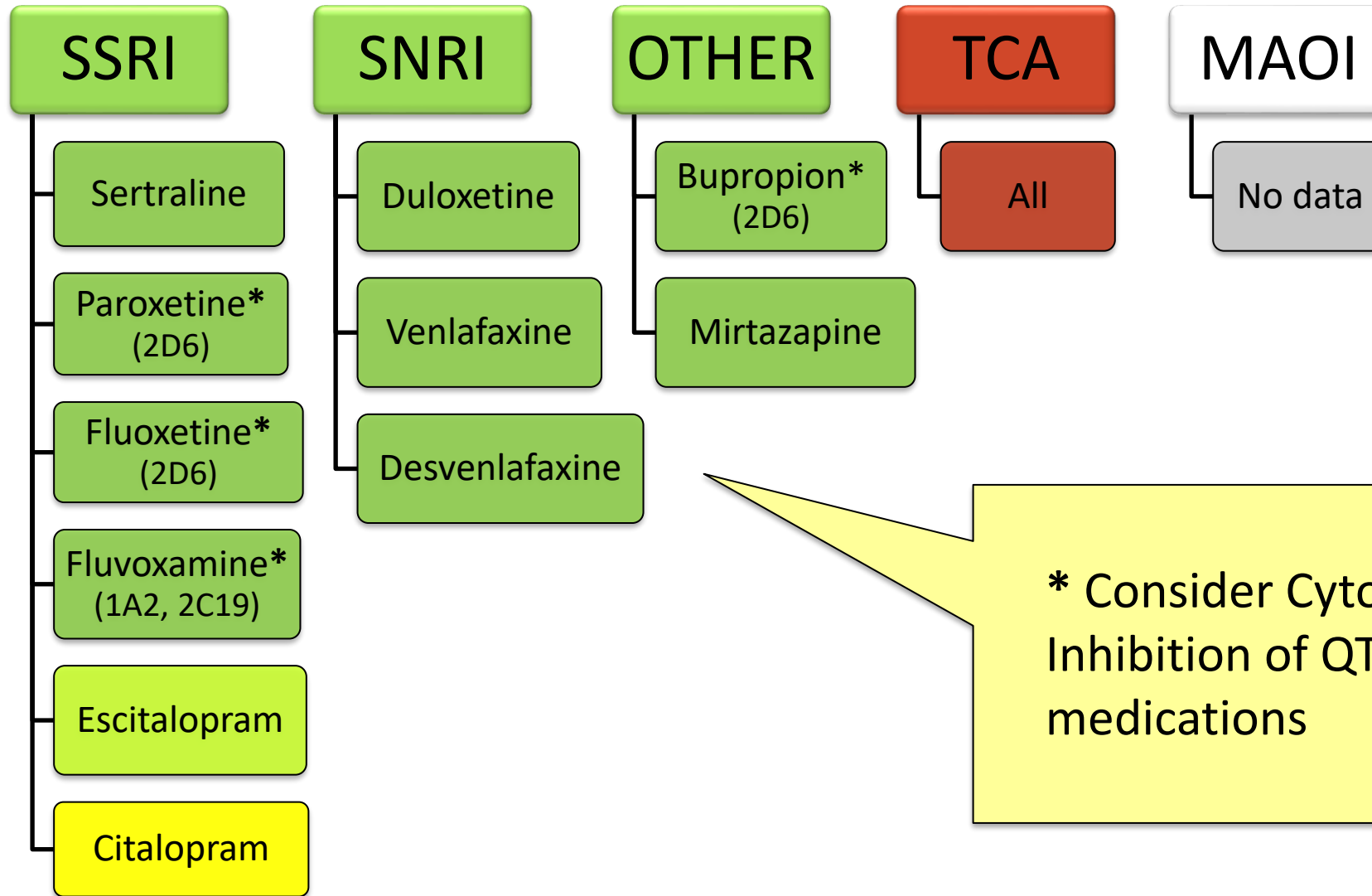
Critical Appraisal of the  
Literature is Essential!



# PSYCHOTROPIC MEDICATIONS



# ANTIDEPRESSANTS



\* Consider Cytochrome p450  
Inhibition of QTc-prolonging  
medications

## August 2011: FDA Drug Safety Communication

- Citalopram ***should not be prescribed*** at doses > 40mg
- Citalopram should not be used at doses > 20mg in those with liver dysfunction or over age 60
- FDA asserts 60mg no more efficacious than 40mg
- Single study showing increase of 8.5 ms at 20mg and 18.5 ms at 60mg
- Similar study w/escitalopram (4.5 ms at 10mg and 10.7 ms at 30mg) but no recommendations from FDA

## March 2012: FDA Revised Recommendation

- Citalopram ***not recommended*** at doses > 40mg
- Citalopram should be discontinued in anyone w/ QTc>500 ms

# Cardiac risk of using citalopram?



All cause hospitalization and death significantly **increased** after citalopram dose reduction

No difference risk of VT/VF/sudden cardiac death vs other SSRIs

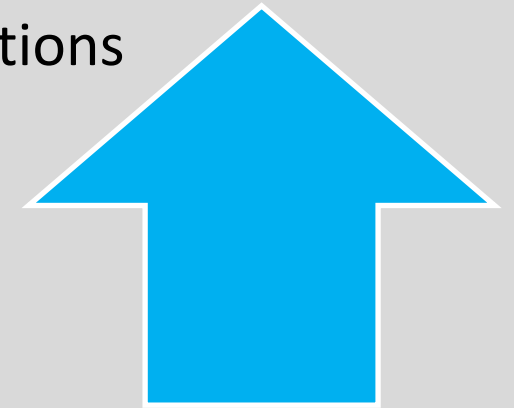


Hospitalizations for depression significantly ↑ after dose reductions

Increased prescriptions for interacting medications

More likely to be prescribed sedatives or anxiolytics

Higher healthcare utilization



## Risk of reflexively reducing citalopram dose?

# ANTIPSYCHOTICS



## Lowest risk:

- lurasidone
- aripiprazole



## Low to Moderate risk:

- haloperidol
- quetiapine
- olanzapine
- risperidone



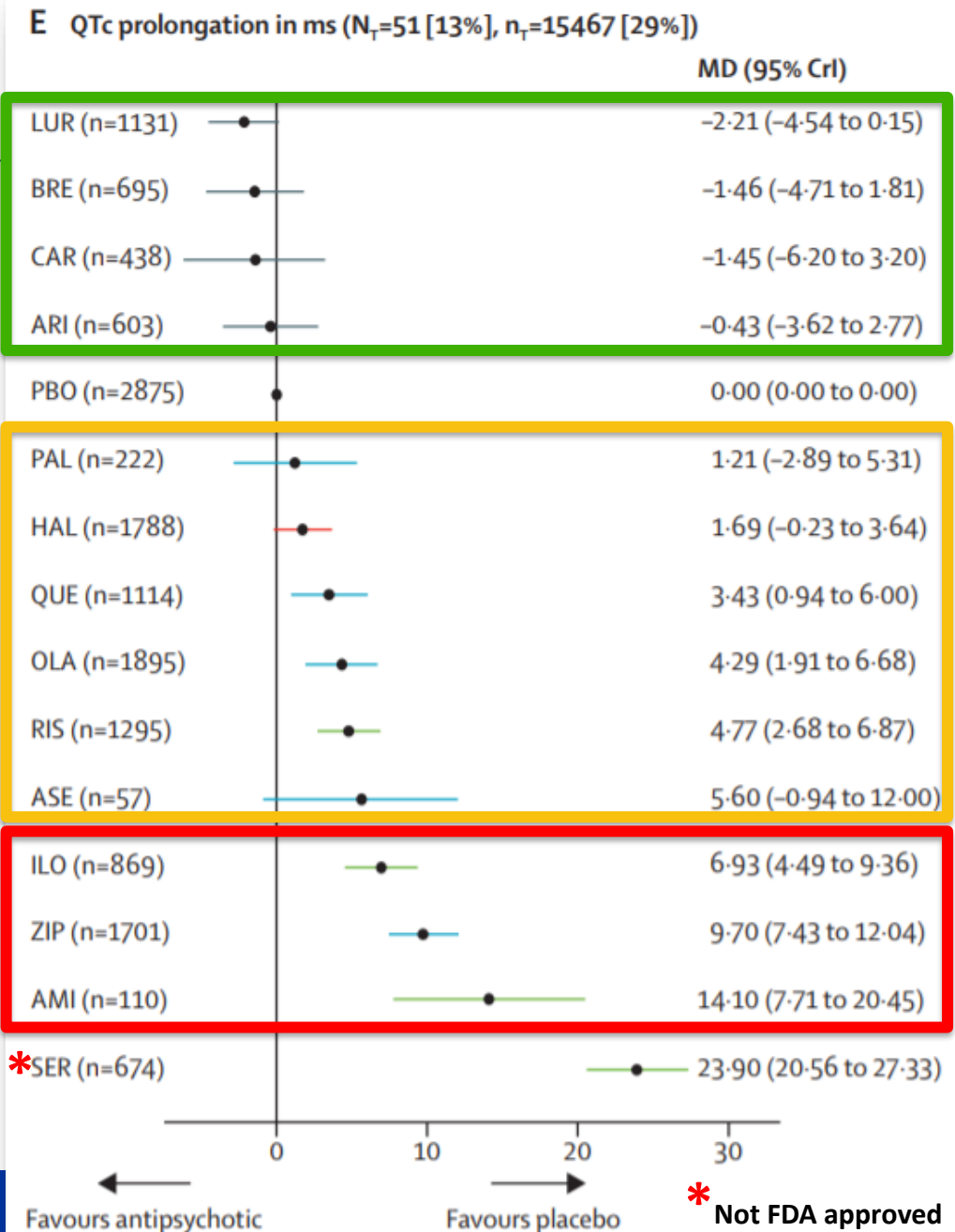
## Higher risk:

- iloperidone
- ziprasidone
- typicals (low potency phenothiazines: thioridazine, chlorpromazine, mesoridazine)



## Not enough data:

- clozapine (likely low risk)





Contents lists available at [ScienceDirect](#)

## General Hospital Psychiatry

journal homepage: [www.elsevier.com/locate/genhospsych](http://www.elsevier.com/locate/genhospsych)

Review article

Intravenous haloperidol: A systematic review of side effects and recommendations for clinical use

Scott R. Beach<sup>a,\*</sup>, Anne F. Gross<sup>b</sup>, Kimberly E. Hartney<sup>c</sup>, John B. Taylor<sup>a</sup>, James R. Rundell<sup>d</sup>

- 2007 FDA warning suggested increased risk and recommended ECG monitoring for patients receiving IV haloperidol
- However, there is a paucity of data



- Studies of IV haloperidol recipients have confounders
  - severe medical illness, including electrolyte disturbance
  - underlying cardiac illness
  - multiple QT-prolonging medications
- Recommendations for use in Inpatient Setting
  - Check baseline ECG and at least one follow-up
  - Consider daily ECG if other risk factors are present
  - Ensure repletion of electrolytes and minimize other risk factors
  - For QTc > 500 ms, consider continuous monitoring or alternative agents
  - Remember: the ICU is the safest place in the hospital



## Do not significantly prolong QT interval

- Valproate may have some protective effects and stabilization of cardiac conduction
- There is no evidence to suggest QTc prolongation with:
  - Carbamazepine
  - Oxcarbazepine
  - Topiramate
  - Lamotrigine
  - Gabapentin

However, as these are sodium channel blockers, be aware of risk of conduction delay in patients with BBB.

## ? Lithium's effects on QT remain uncertain

- Only a few small studies
- No QTc prolongation within the therapeutic range of 0.6-1.2 mEq/L
- Increasing serum lithium concentrations correlated w/ QTc prolongation
- QTc increases are modest and may not be clinically significant



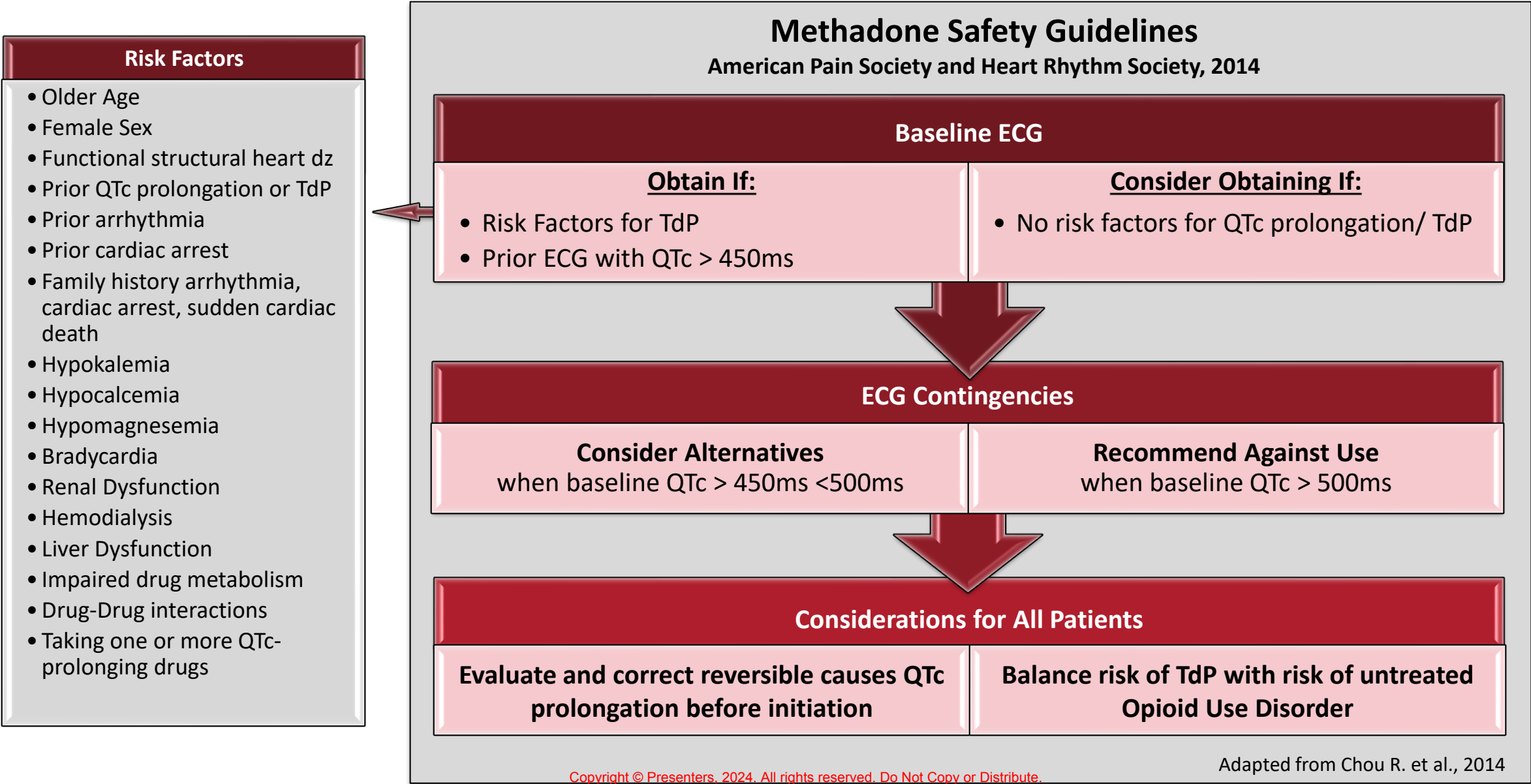
- Prolongs the QTc and is in **highest risk categories for TdP**
- Potent inhibitor of hERG IKr channels
- **2006: FDA issued black box warning:**

**“cases of QT interval prolongation and serious arrhythmia (TdP) have been observed during treatment with methadone”**

**Important to balance risk of TdP and risk of death from OUD!**



# METHADONE SAFETY GUIDELINES



# BUPRENORPHINE

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Safer alternative to methadone

- Does not prolong the QT interval or have an association with TdP
- One hundred times less potent of an hERG IKr inhibitor than methadone

# CONSIDERATIONS FOR ECG MONITORING

## **If using a prior ECG...**

- No more than one month prior to the decision point
- Without substantial changes in medications, electrolytes, or cardiovascular status

## **If in resource-poor areas...**

- Practitioners should not let the absence of an ECG preclude the prescription of a psychiatric medication
- If an ECG machine is available, practitioners of any medical specialty should be comfortable with QTc measurement, calculation and documentation

## Who can interpret an ECG?

- In settings where clinicians do not have access to a cardiology overread, clinicians of any medical specialty should feel comfortable with the measurement, calculation and documentation of the QTc interval



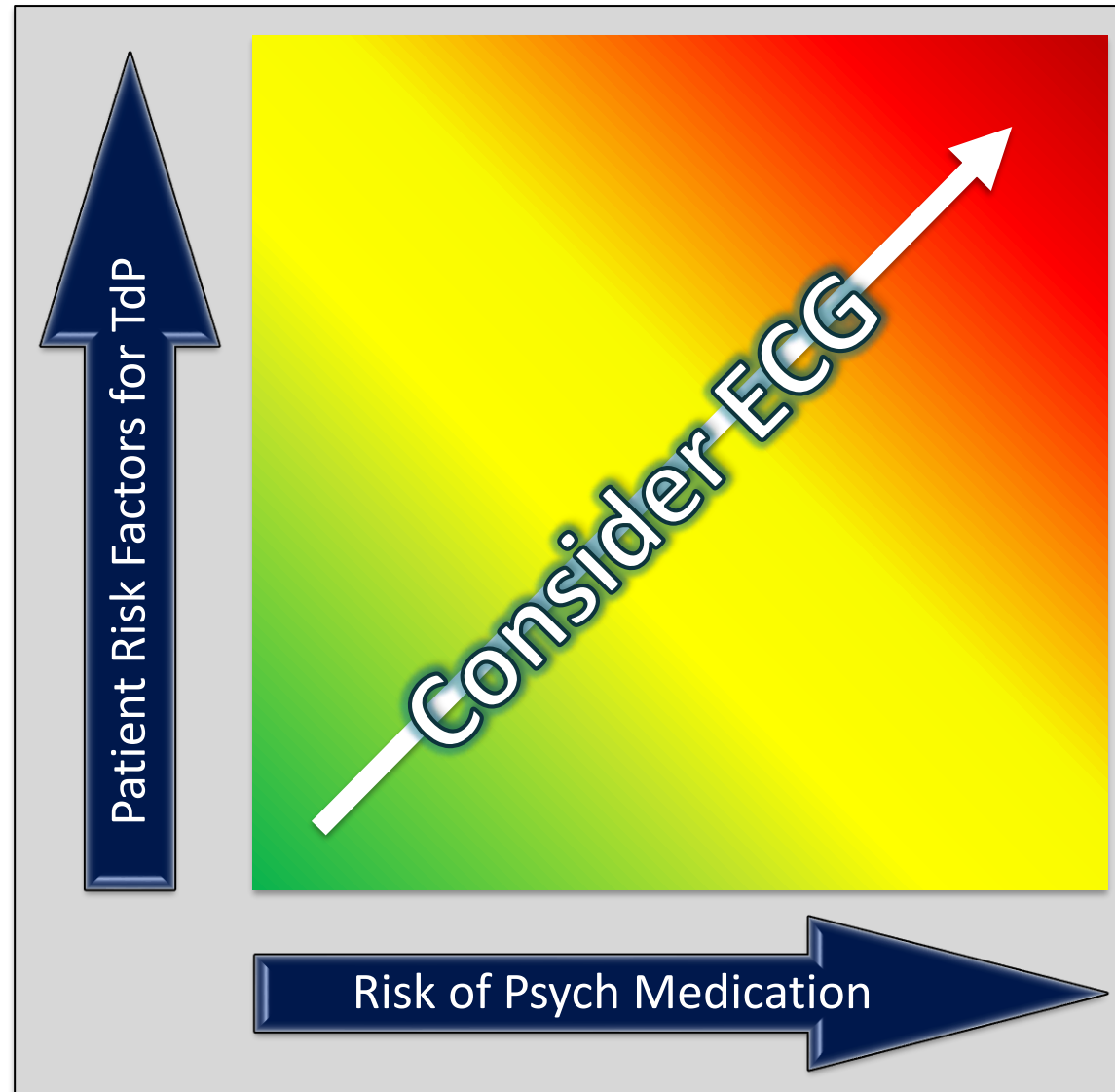
# WHEN TO OBTAIN AN OUTPATIENT ECG?

## Non-Modifiable Risk Factors For TdP

- Older Age
- Female Sex
- Functional structural heart disease
- Prior QTc prolongation or TdP
- Prior arrhythmia
- Prior cardiac arrest
- Family history arrhythmia, cardiac arrest, sudden cardiac death

## Modifiable Risk Factors For TdP

- Hypokalemia
- Hypocalcemia
- Hypomagnesemia
- Bradycardia
- Renal Dysfunction
- Hemodialysis
- Liver Dysfunction
- Impaired drug metabolism
- Drug-Drug interactions
- Taking one or more QTc-prolonging drugs



## Low Risk Medications

- Most SSRIs & SNRIs
- Benzodiazepines
- Valproic Acid
- Buprenorphine
- Aripiprazole
- Lurasidone

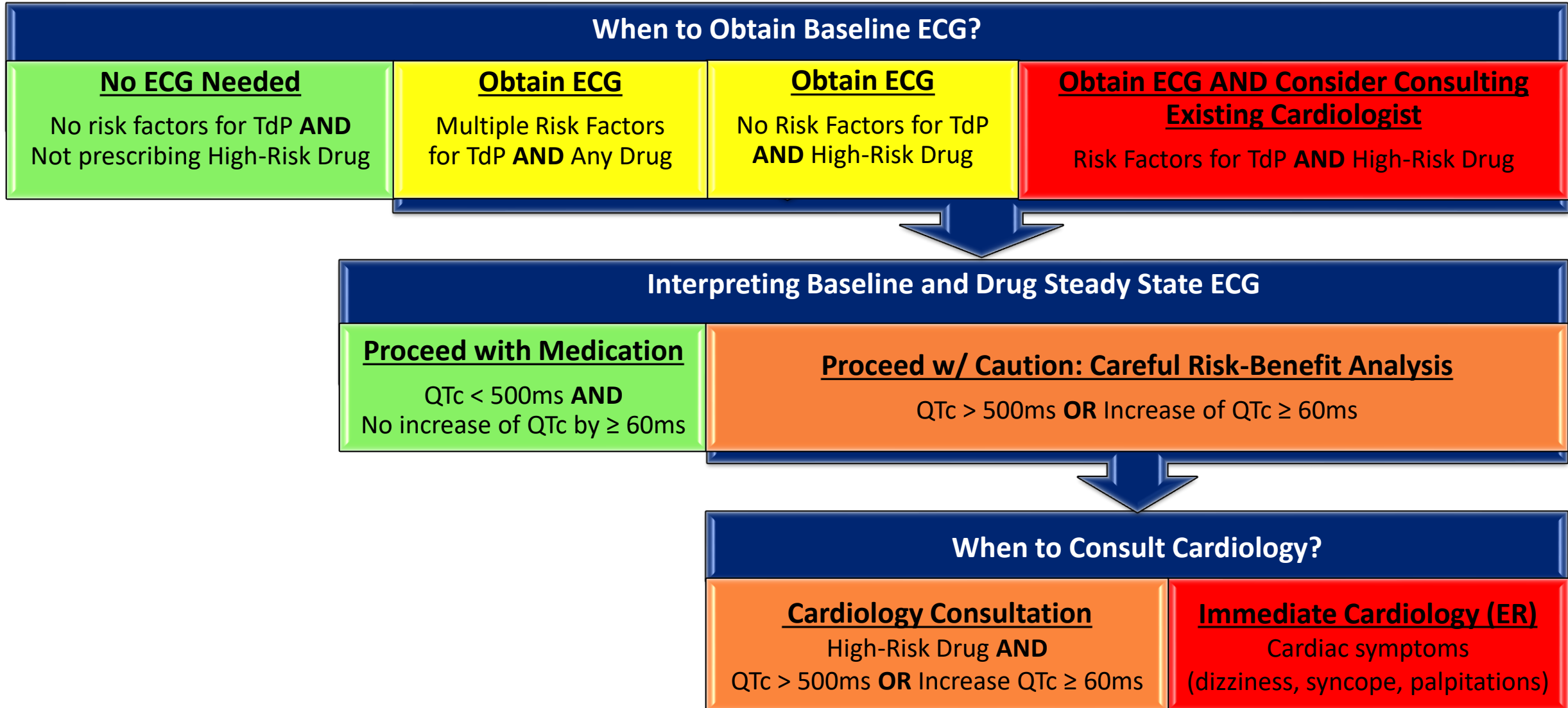
## Moderate Risk Medications

- Citalopram
- Quetiapine, Risperidone, Olanzapine, Haloperidol
- Trazodone

## High Risk Medication

- Methadone
- Ziprasidone
- Iloperidone
- Low -Potency Phenothiazines
- Tricyclic Antidepressants

# CONSIDERATIONS FOR OUTPATIENT ECG MONITORING



# ROLE OF PACEMAKERS AND DEFIBRILLATORS

## CASE 2

44 y/o man with a family history of cardiac arrest in his grandfather, father, and paternal aunt, tests positive for a genetic cardiomyopathy with high risk for sudden cardiac death. He has never had any arrhythmias or cardiac symptoms. He is implanted with a subcutaneous Implantable Cardioverter Defibrillator (ICD) for primary prevention.

His past medical and psychiatric history is notable for hyperlipidemia, recurrent sinus infections, and depression. He takes simvastatin, escitalopram, and is frequently prescribed a Z-pack (azithromycin) by his PCP.

He develops a viral GI illness with multiple days of vomiting and diarrhea, not able to keep anything down. He presents to the ED for dehydration where his QTc(H) is 522ms, K<sup>+</sup> is 2.7. The ED resident orders zofran for nausea. When another ED resident questions this decision due to Torsades risk, the first resident says “Don’t worry about it. He has an ICD.”

## Should they worry about it?

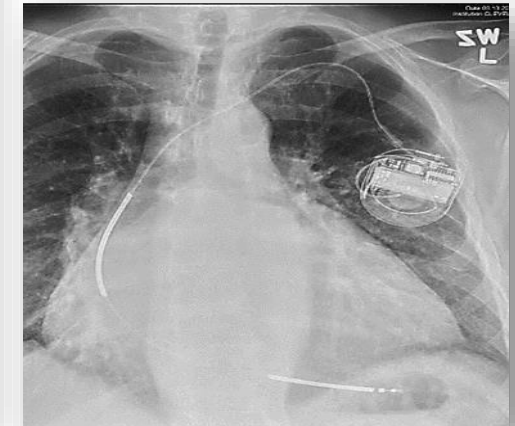
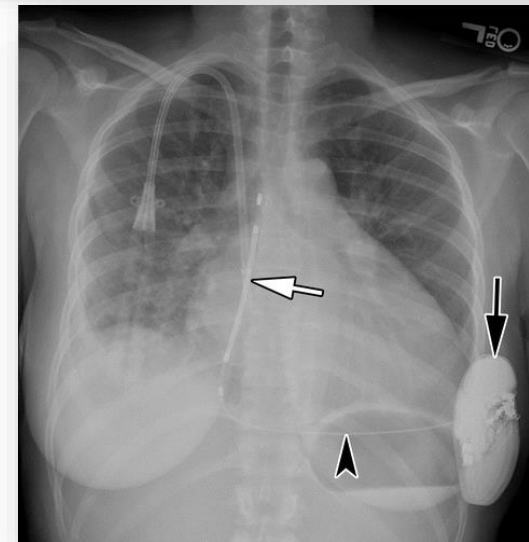
# INDICATIONS FOR ICD IMPLANTATION

## Primary Prevention:

- CAD + Heart failure LVEF  $\leq 35\%$
- Dilated Cardiomyopathy
- Certain Pathogenic Gene Mutations
- Arrhythmogenic RV Cardiomyopathy
- Congenital Long QT Syndrome
- Asymptomatic QTc  $> 500\text{ms}$  during  $\beta$ -Blocker
- Brugada syndrome + symptoms/ inducible AF

## Secondary Prevention:

- VF sudden cardiac arrest
- sustained VT
- Hemodynamically not-tolerated VT

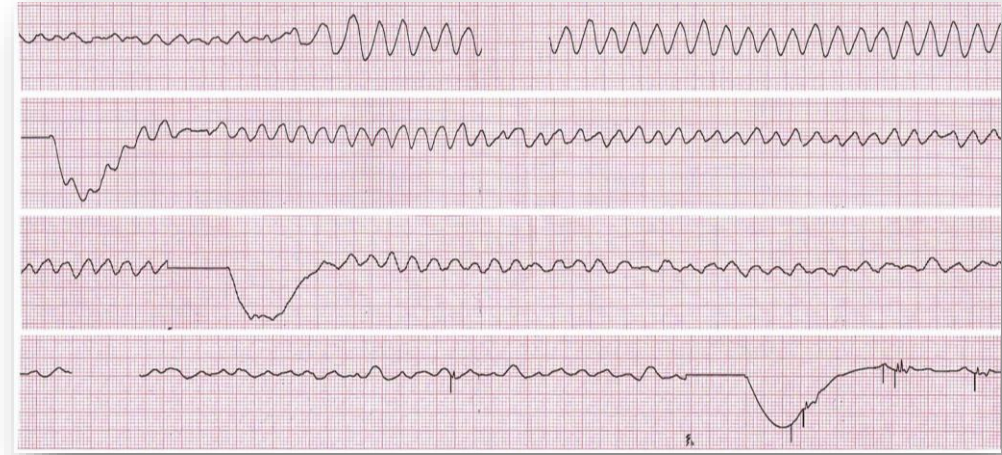






## ICDs can readily terminate most VT/VF effectively, but...

- Even appropriate shocks are independently associated with increased risks of death and worsening heart failure
- Some VT will recur if substrates are unchanged, despite “successful” shocks
- ICD “storms” are common, which lead to significant psychological morbidity

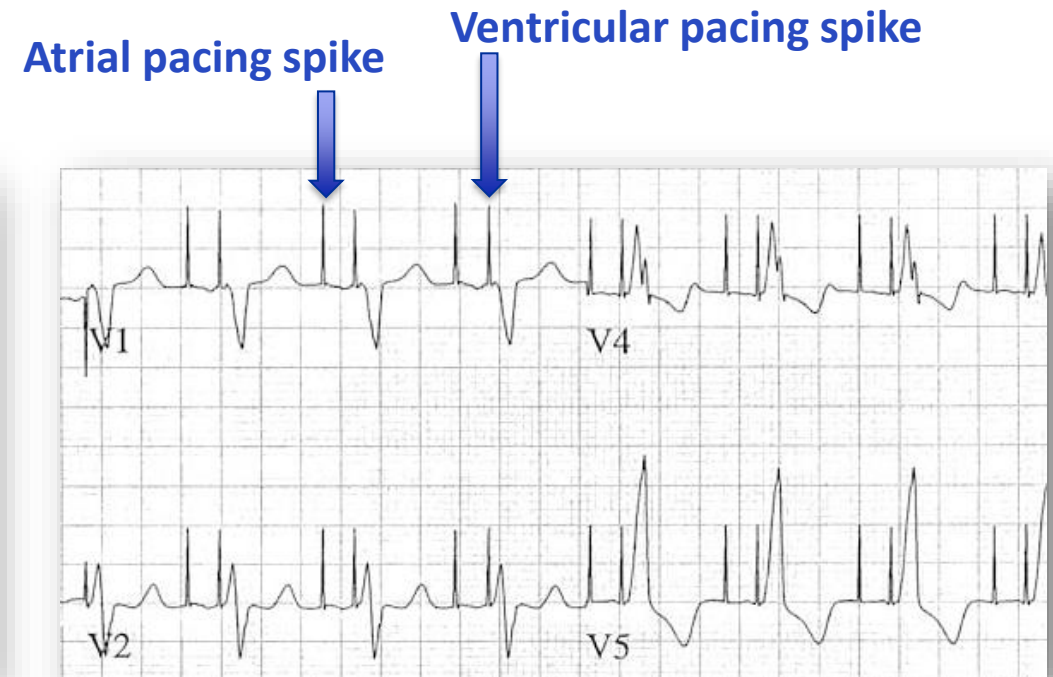
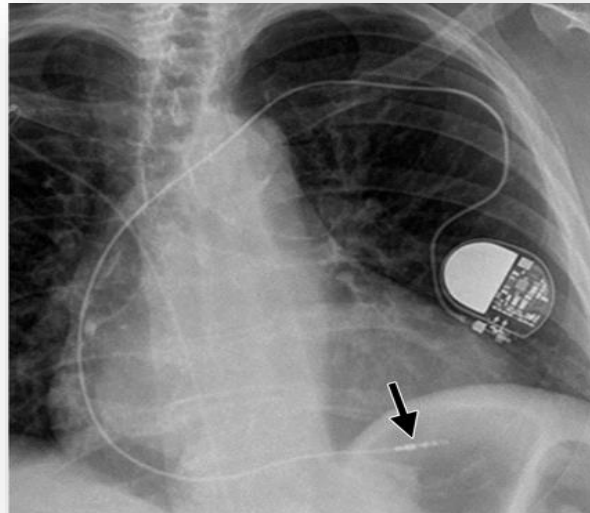


# PERMANENT PACEMAKER (PPM)

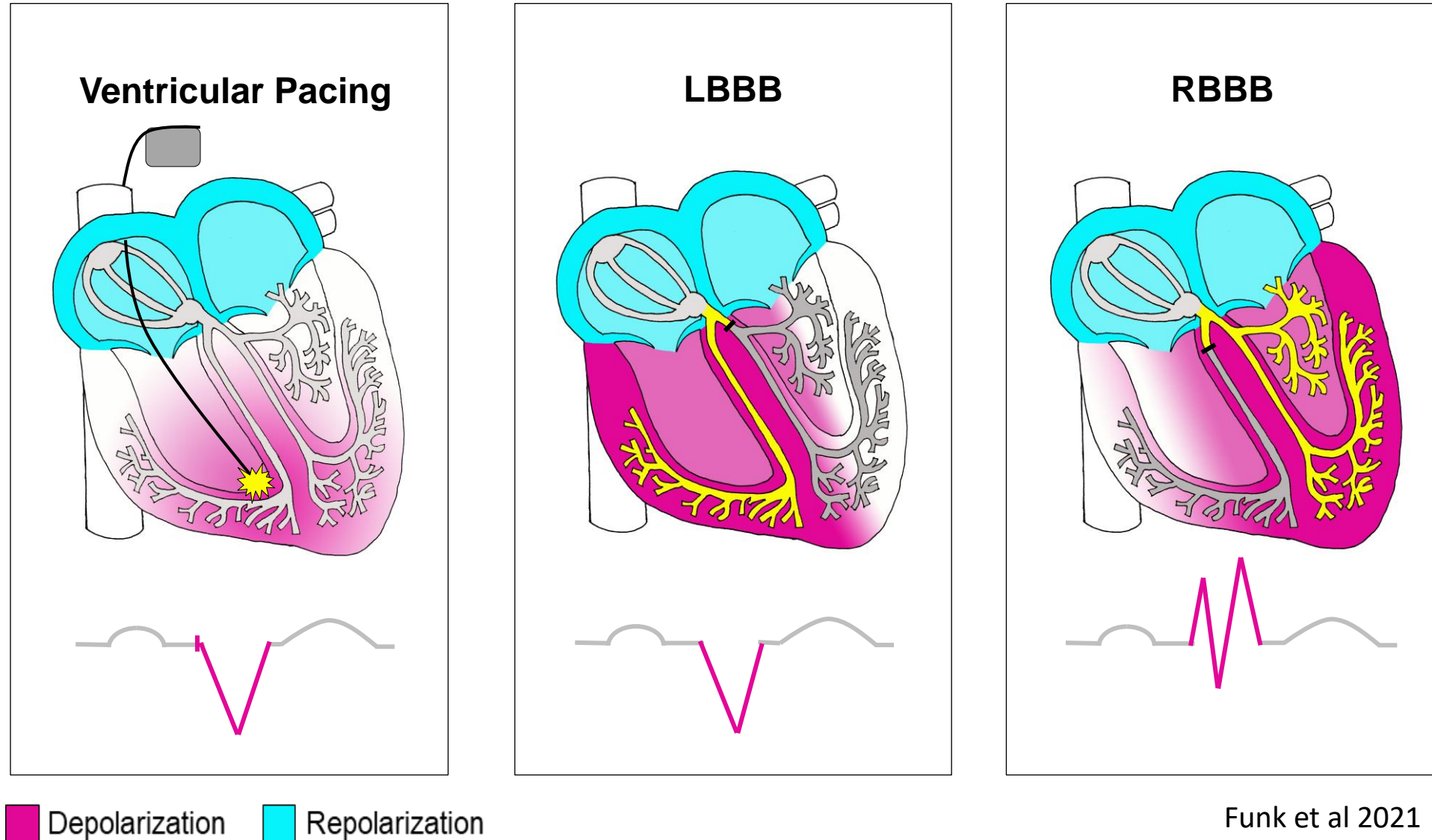
**Indication:** treatment of brady-arrhythmias

**Goal:** to sustain adequate HR for daily activity

**How does it work?** Paces the heart if the HR drops below the pacing threshold (usually 30-40 bpm)



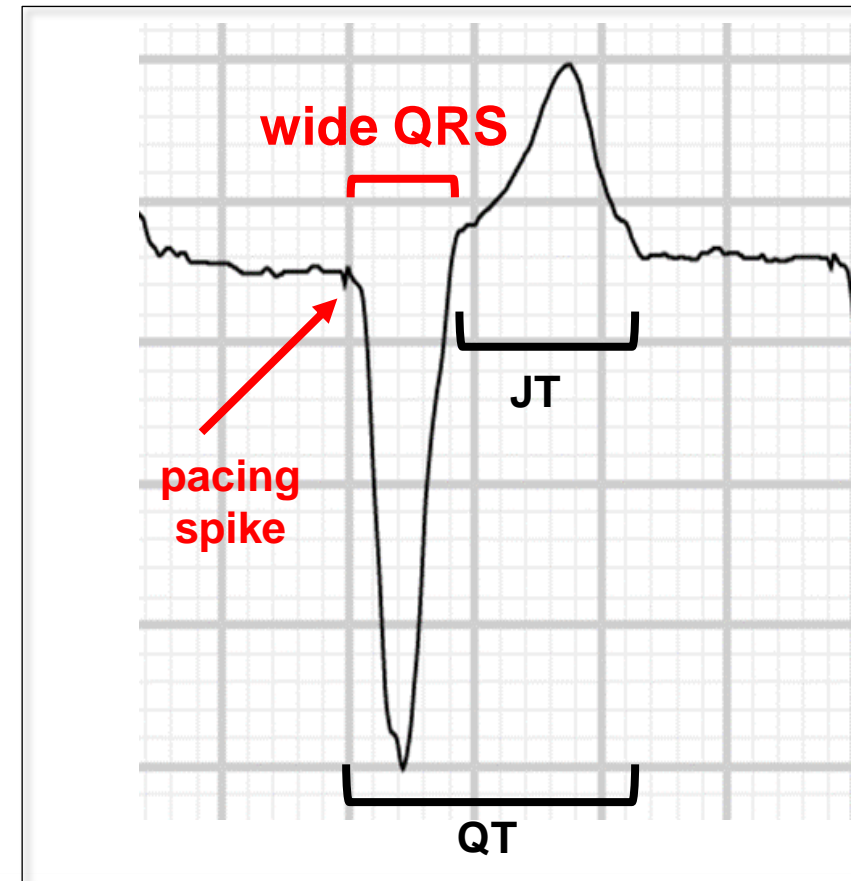
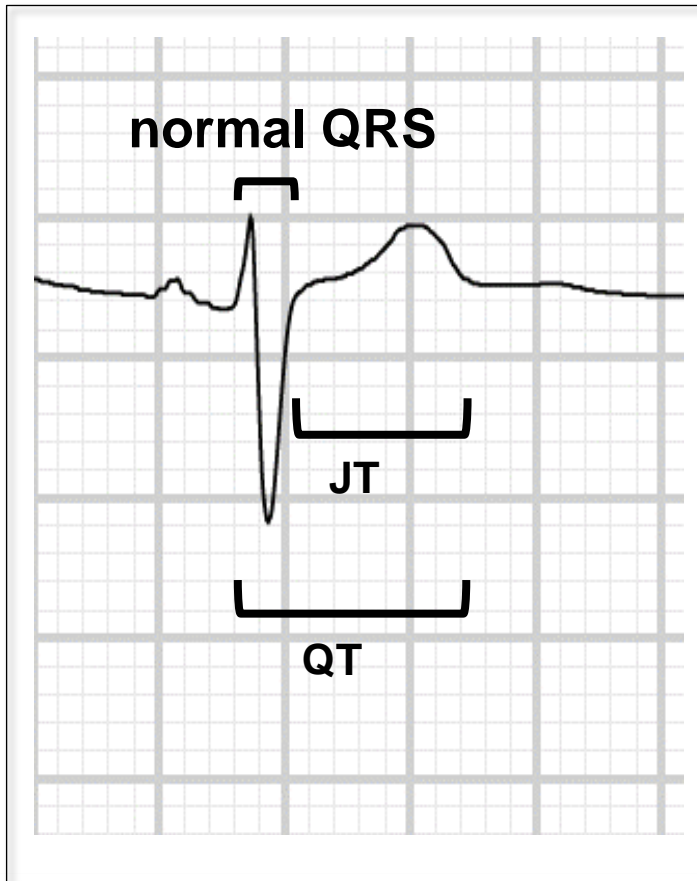
# PERMANENT PACEMAKER (PPM)



Funk et al 2021



# WIDE QRS: VENTRICULAR PACING OR BBB



**Widening of QRS leads to prolongation of QTc without perturbation of repolarization**

# CASE 3

A 63 y/o woman with MDD and GAD presents for a new patient evaluation in your outpatient psychiatry clinic. Past medical history notable for:

- rheumatic fever, c/b mitral & aortic valve stenosis
- s/p mitral and aortic valve replacement
- HFpEF
- atrial fibrillation on amiodarone and warfarin
- right bundle branch block
- obesity
- other meds: furosemide

She has suffered from terrible depression since the death of her sister by suicide 9 months ago. + low mood, anhedonia, passive thoughts of death, amotivation, hopelessness, & extreme guilt. Feels paralyzed by worry, can't tolerate being around people. Has daily panic attacks.

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She has never had a trial of an SSRI.



Vent. rate  
PR interval  
QRS duration  
QT/QTc

57 BPM

\* ms

144 ms

520/506 ms

Atrial fibrillation with slow ventricular response

Right axis deviation

Intraventricular conduction defect

Abnormal ECG

## Atrial Fibrillation

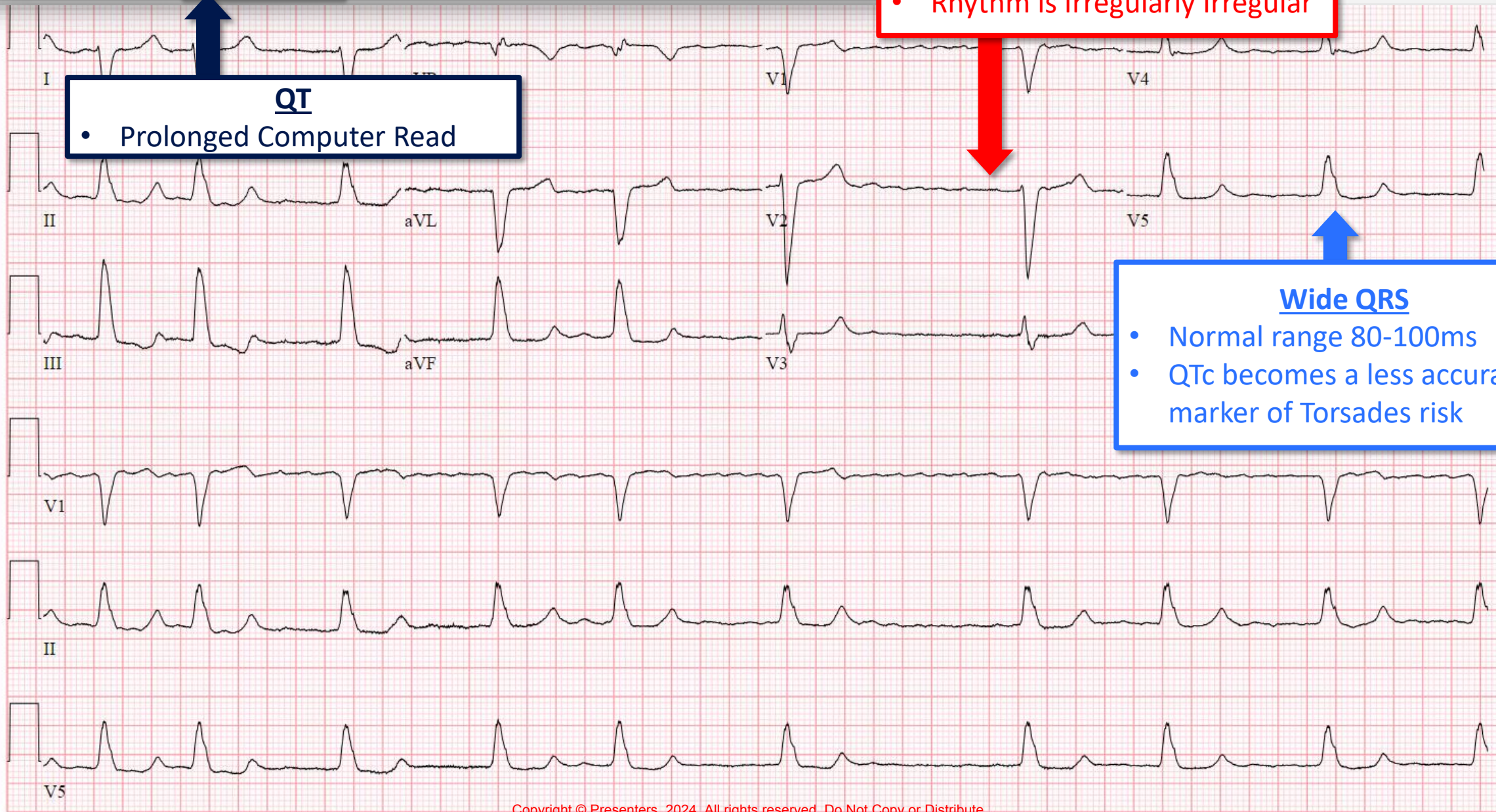
- Absence of p-waves
- Rhythm is Irregularly Irregular

## QT

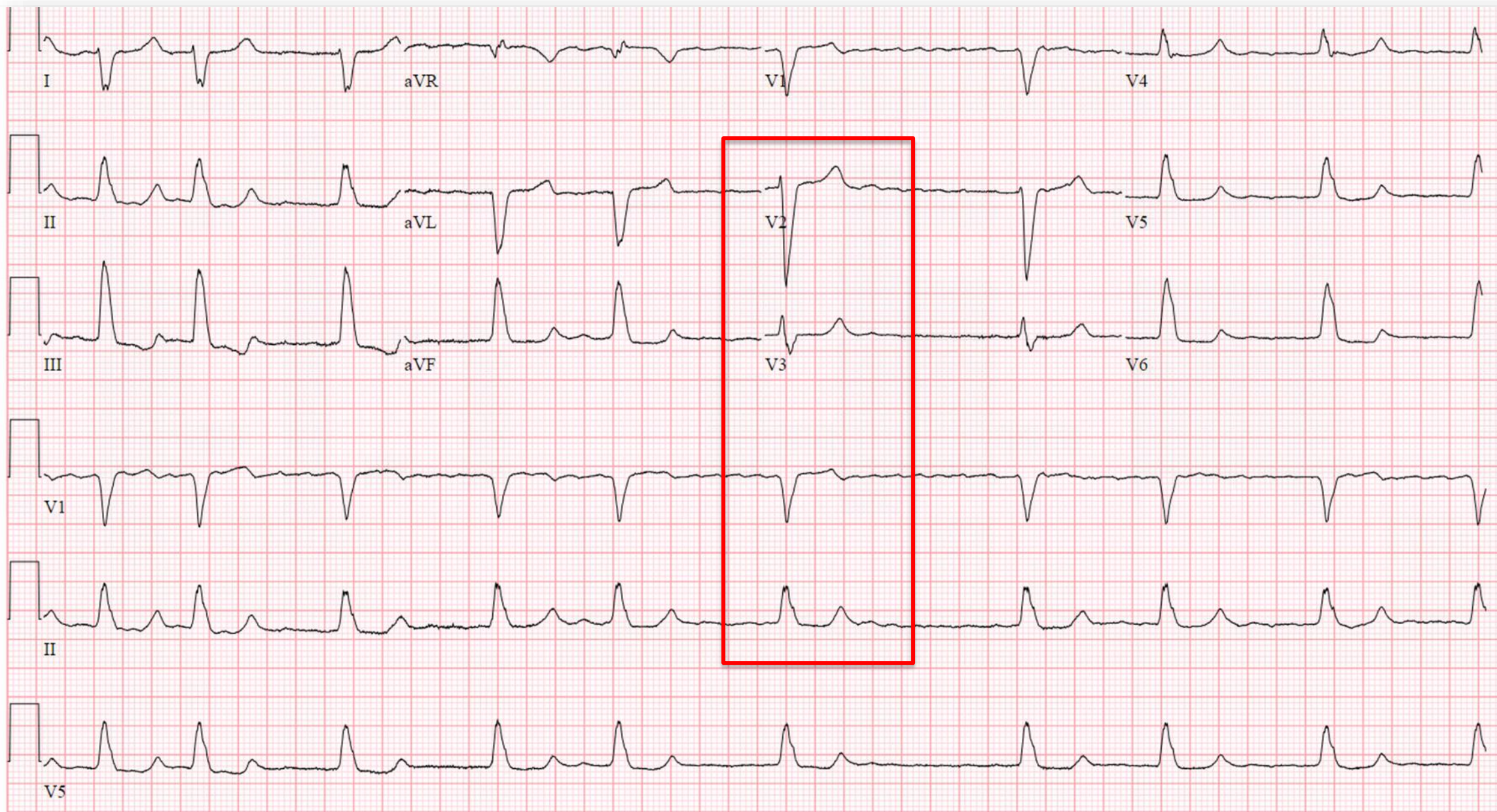
- Prolonged Computer Read

## Wide QRS

- Normal range 80-100ms
- QTc becomes a less accurate marker of Torsades risk

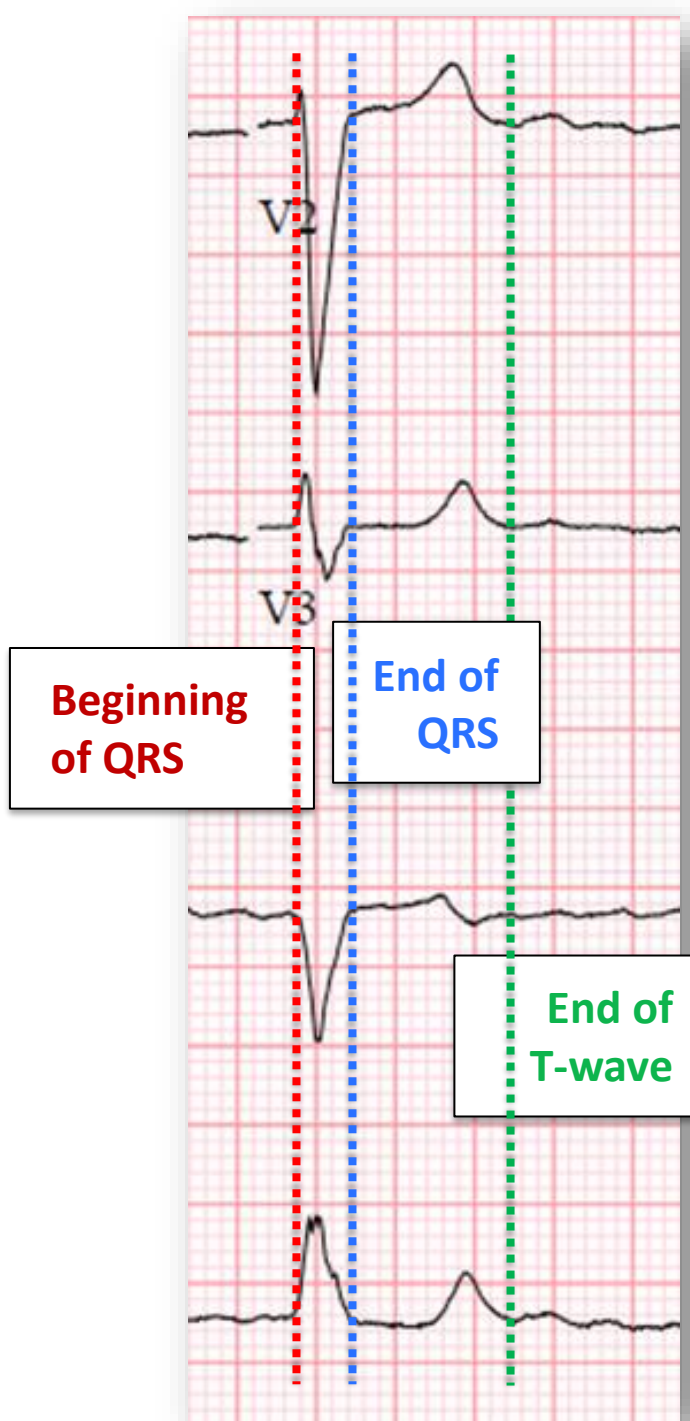


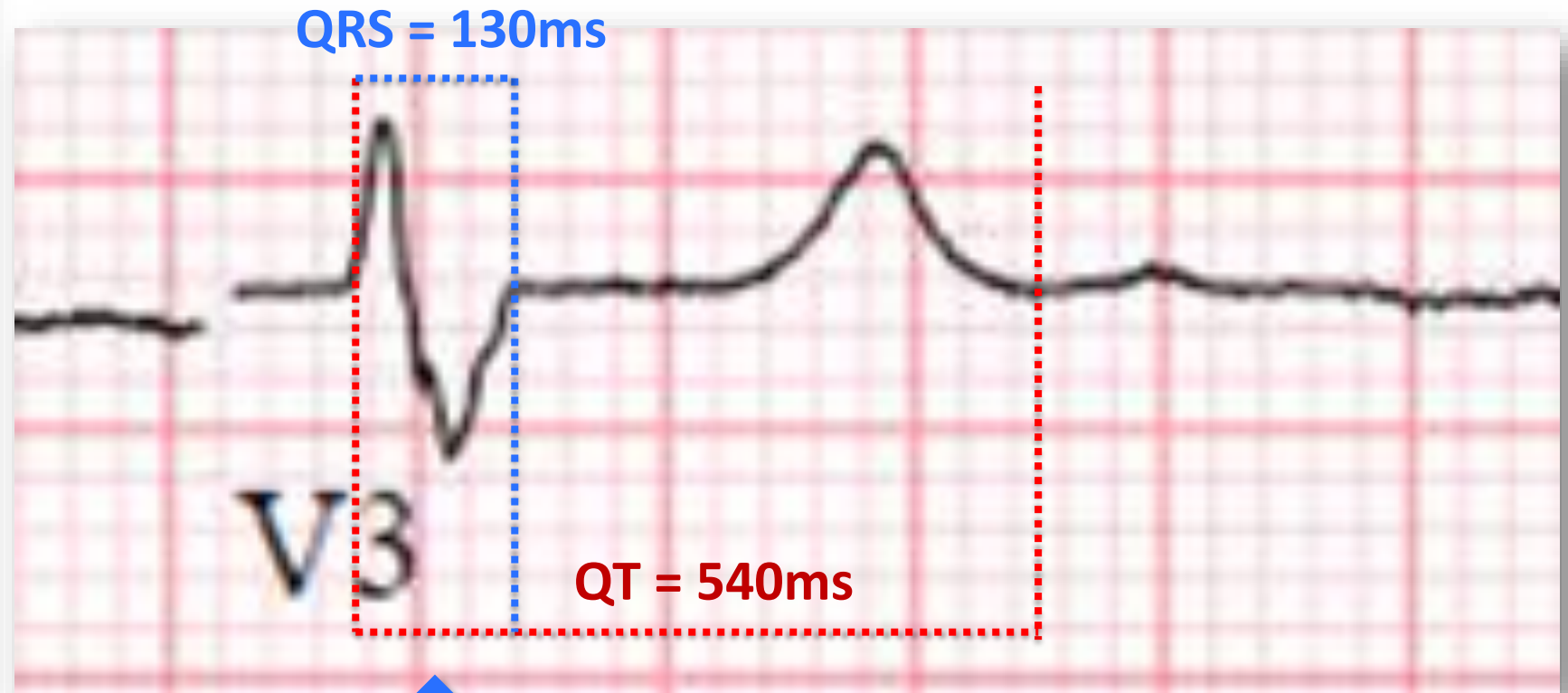
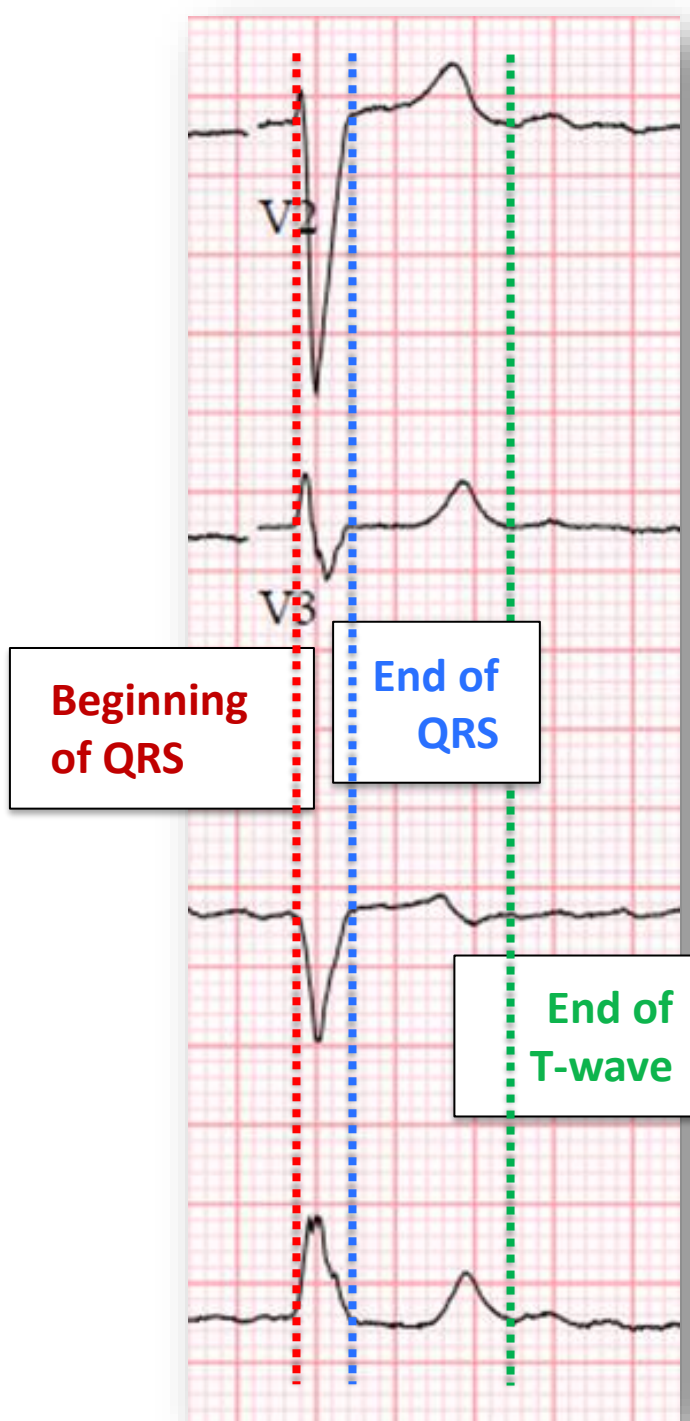






# What is the QT interval?

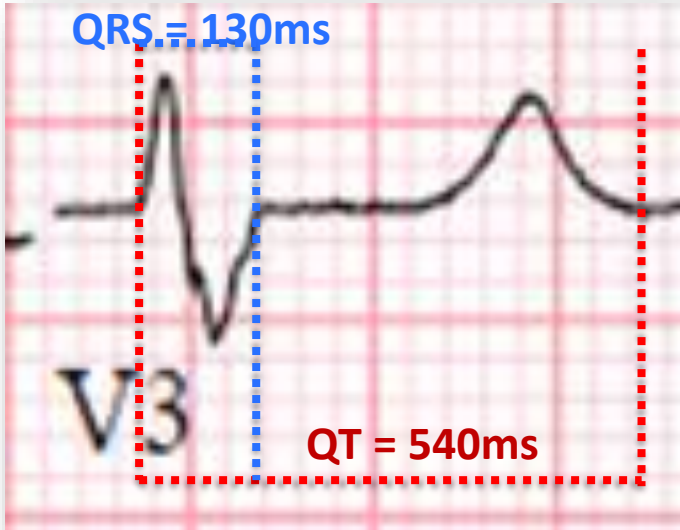
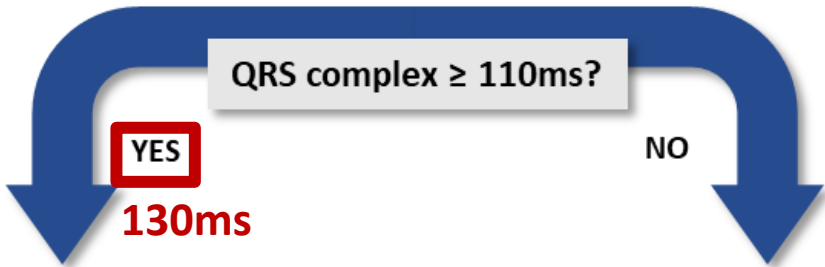




**Widening of QRS leads to prolongation of QTc without perturbation of repolarization**

# CORRECTING FOR WIDE QRS

## STEP 1: Obtain ECG Measurements (QT, QRS, RR/HR)



## STEP 2: Select Wide QRS Correction Method

BOGOSSIAN SIMPLIFIED  
 $QT_m = QT - 0.5 \times QRS$

JT INTERVAL  
 $JT = QT - QRS$

$QT_m$  = QT modified for wide QRS

$$QT_m = 540 - 0.5 \times 130 = 475\text{ms}$$
$$JT = 540 - 130 = 410\text{ms}$$

## STEP 3: Select Heart Rate Correction Method

HODGES  
 $QT_c = QT_m + 1.75 (HR - 60)$

FRIDERICIA  
 $QT_c = QT_m / \sqrt[3]{RR}$

JTc: substitute JT for  $QT_m$

$$QT_c = 475\text{ms} + 1.75 (57 - 60) = 470\text{ms}$$
$$JT_c = 410\text{ms} + 1.75 (57 - 60) = 405\text{ms}$$

## QTc and JTc Upper Limits of Normal

QTc  
500 ms

JTc  
men 355 ms  
women 372 ms

QTc = 470ms  
JTc = 405ms





Vent. rate  
PR interval  
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QT/QTc

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\* ms  
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Atrial fibrillation with slow ventricular response  
Right axis deviation  
Intraventricular conduction defect  
Abnormal ECG

**Atrial Fibrillation**

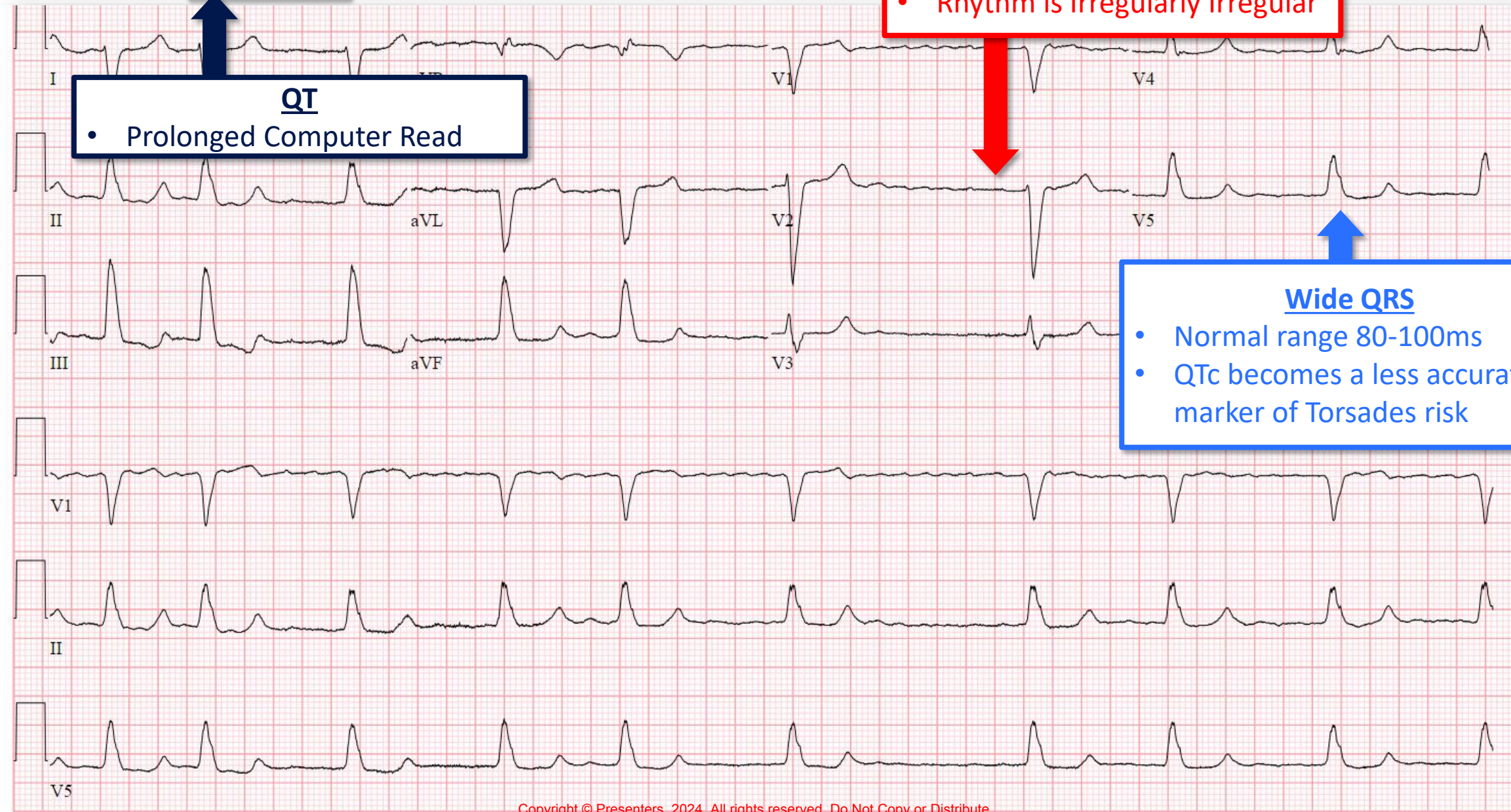
- Absence of p-waves
- Rhythm is Irregularly Irregular

**QT**

- Prolonged Computer Read

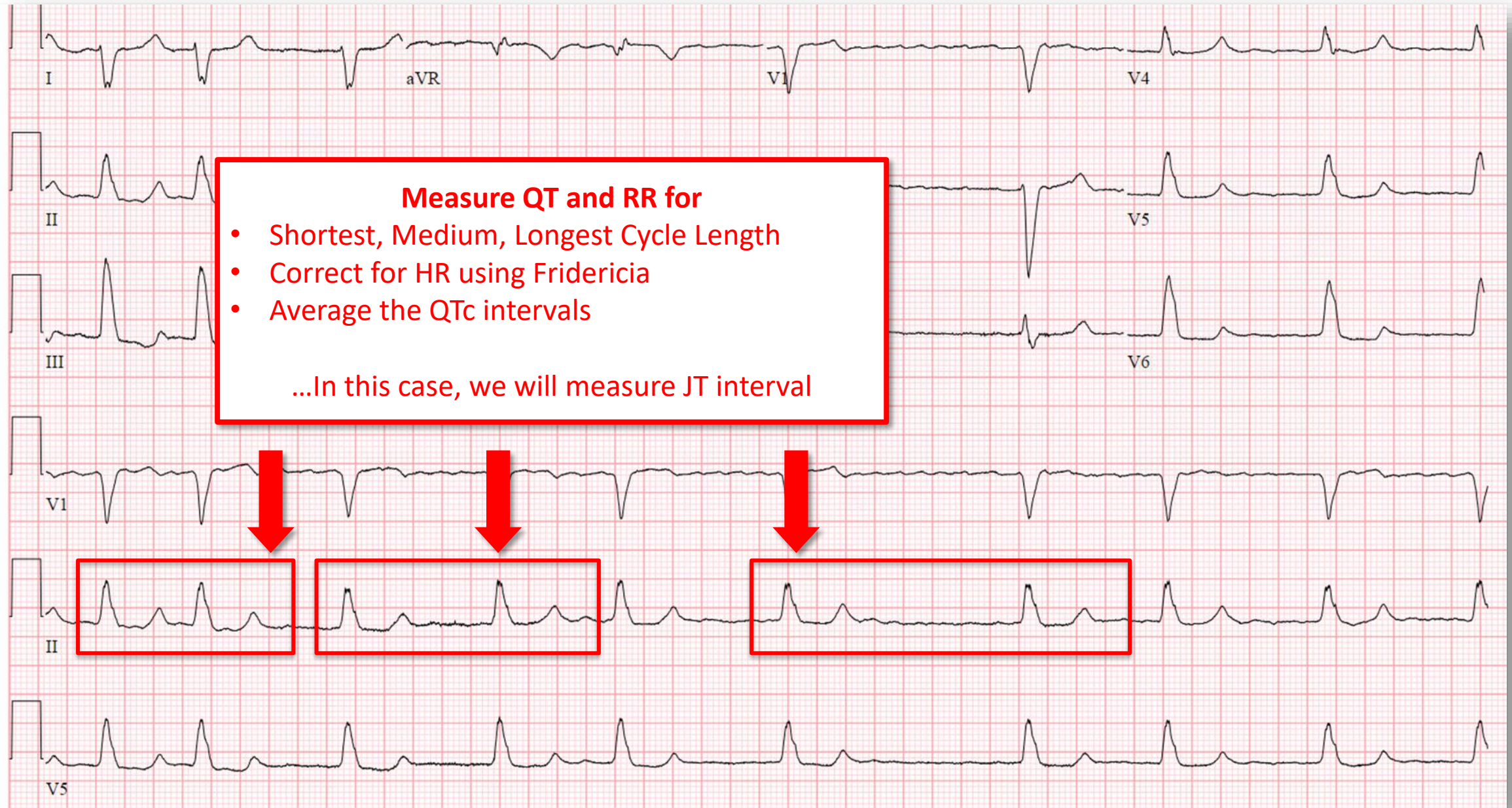
**Wide QRS**

- Normal range 80-100ms
- QTc becomes a less accurate marker of Torsades risk





# QTC IN ATRIAL FIBRILLATION





# QTC IN ATRIAL FIBRILLATION

$$\frac{(JTc_1 + JTc_2 + JTc_3)}{3} = JTc_{\text{mean}}$$

3

$$(464 + 373 + 296) = 378\text{ms}$$

3

RR= 640ms

JT= 400ms

JTc<sub>1</sub> (Frid)= 464ms

JT= 380ms

RR= 1060ms

JTc<sub>2</sub> (Frid)= 373ms

JT= 350ms

RR= 1660ms

JTc<sub>3</sub> (Frid)= 296ms

# CASE 3

A 63 y/o woman with MDD and GAD presents for a new patient evaluation in your outpatient psychiatry clinic. Past medical history notable for:

- rheumatic fever, c/b mitral & aortic valve stenosis
- s/p mitral and aortic valve replacement
- HFpEF
- atrial fibrillation on amiodarone and warfarin
- right bundle branch block
- obesity
- other meds: furosemide

She has suffered from terrible depression since the death of her sister by suicide 9 months ago. + low mood, anhedonia, passive thoughts of death, amotivation, hopelessness, & extreme guilt. Feels paralyzed by worry, can't tolerate being around people. Has daily panic attacks.

Two of her 8 other siblings also ended their lives by suicide. She has had a trials of mirtazapine (oversedation, no mood improvement), and bupropion (worsened her anxiety).

She has never had a trial of an SSRI. **Her JTc is 378ms (upper limit of normal in women = 372ms).**

## Will you prescribe an SSRI?

# RISK STRATIFICATION & MITIGATION

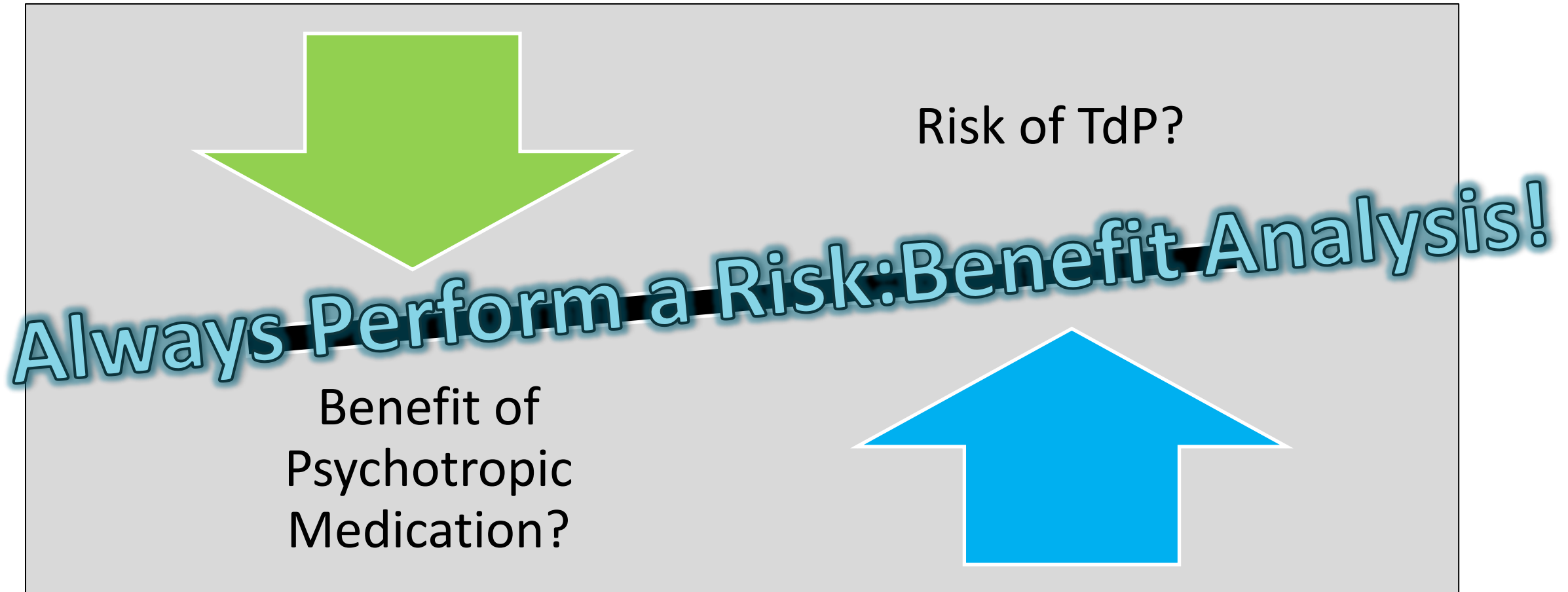
# TYPES OF RISK MITIGATION

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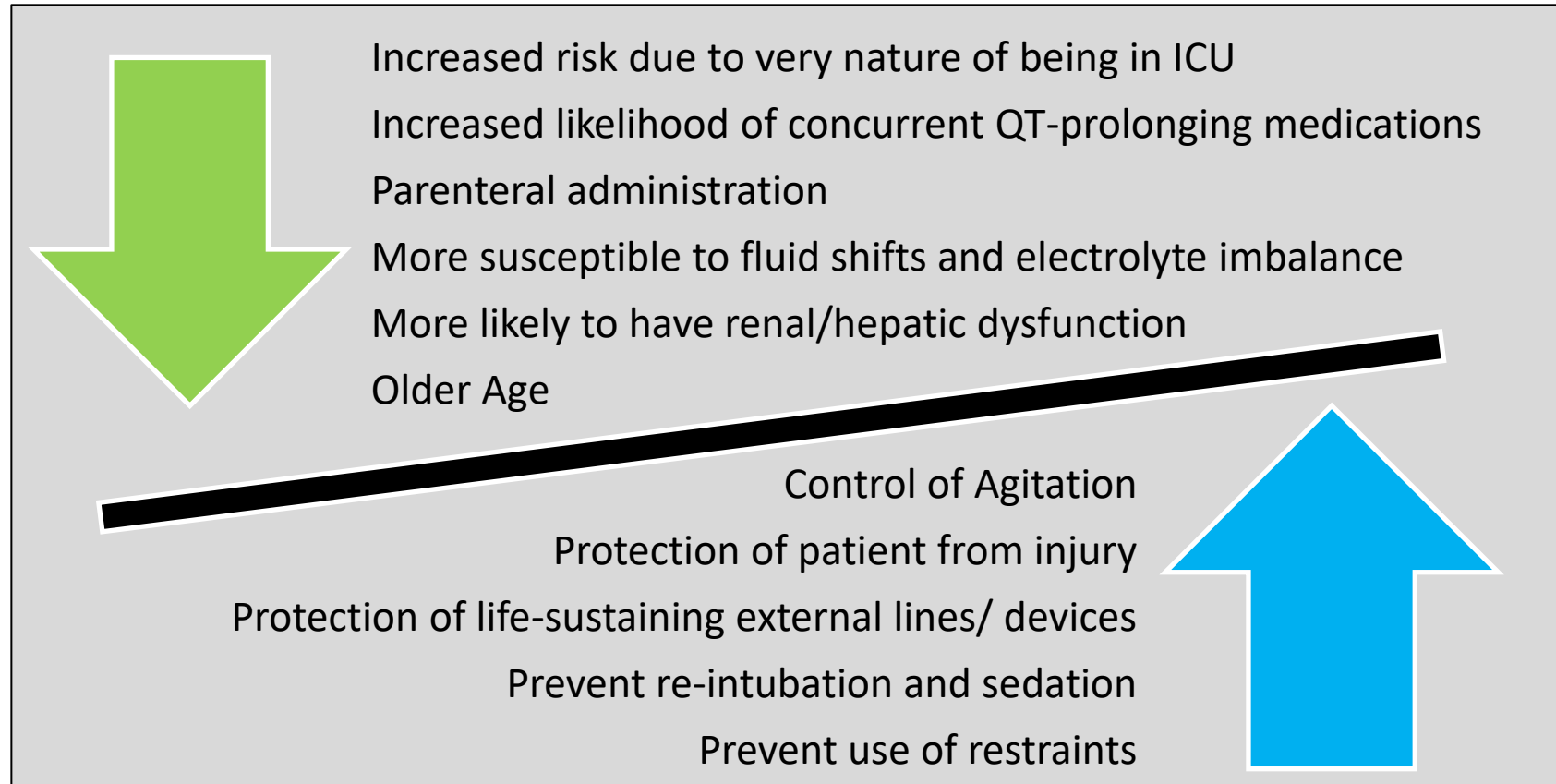
- Comfort measuring QTc and knowing when to adjust your approach (e.g. wide QRS from pacing or BBB)
- How and when to monitor
- Choice of medication
- Involve the other experts
- Interventions for high-risk situations



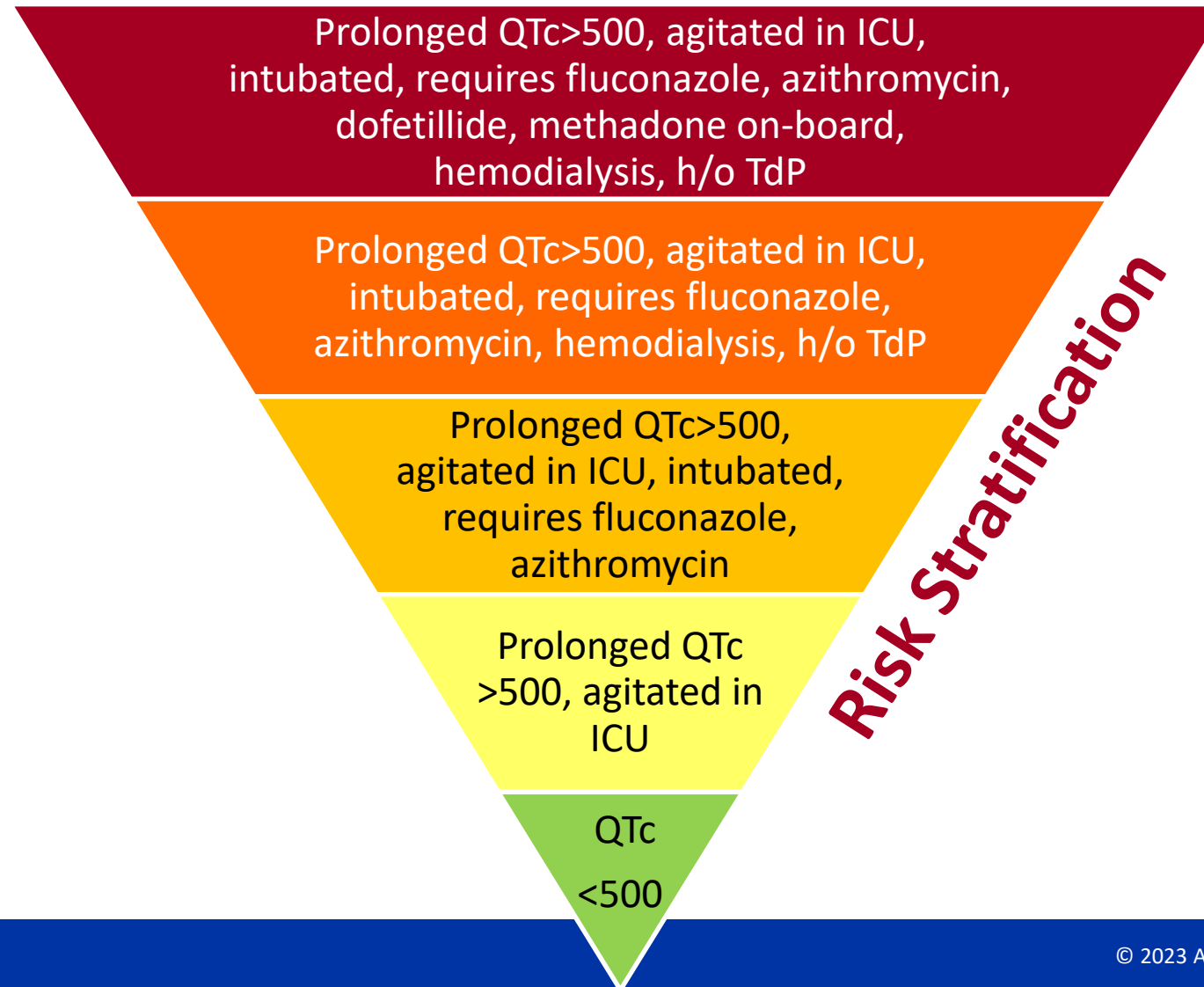
## To Prescribe or Not to Prescribe?



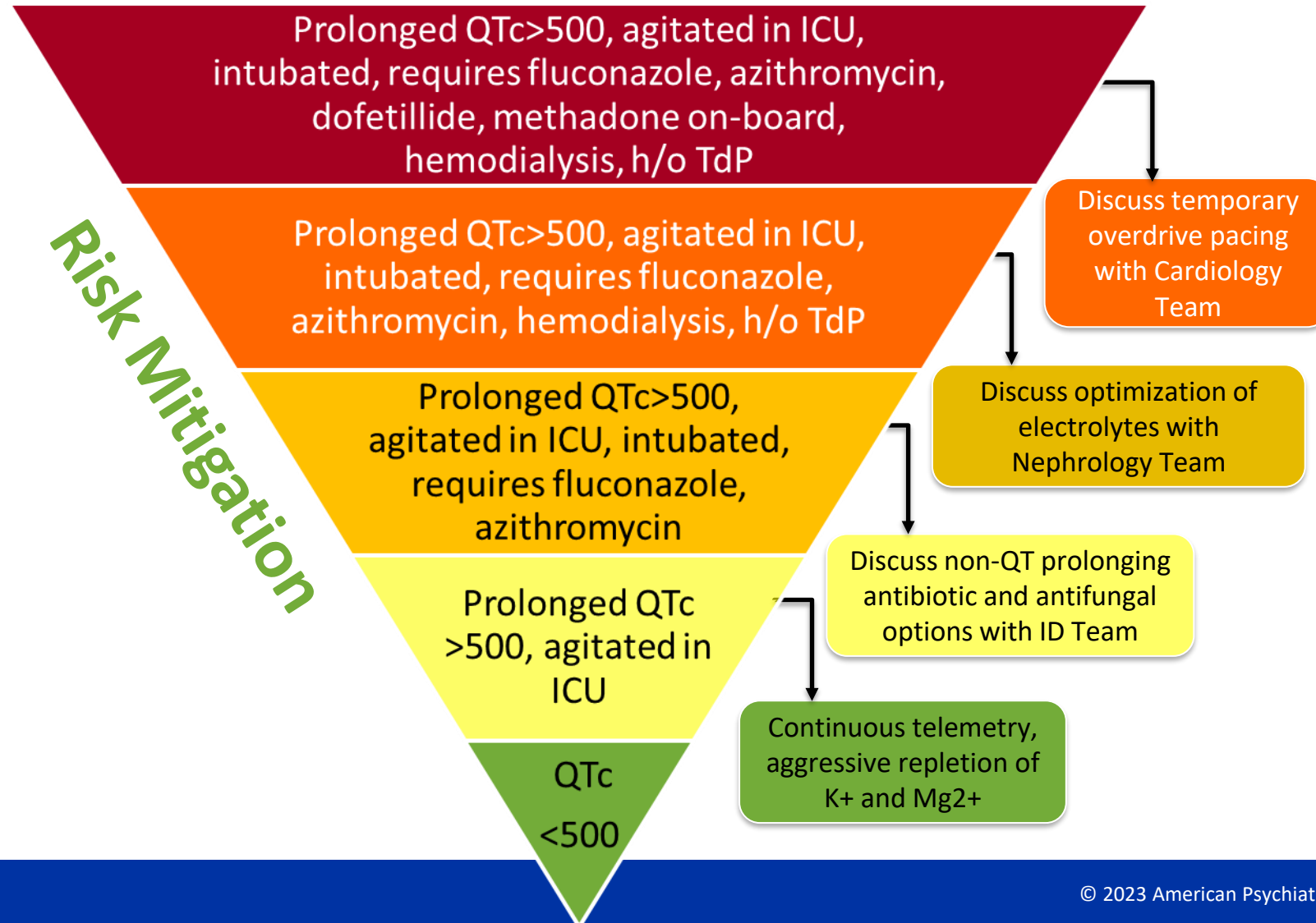
## Risk-Benefit Analysis: ICU



# RISK STRATIFICATION & MITIGATION



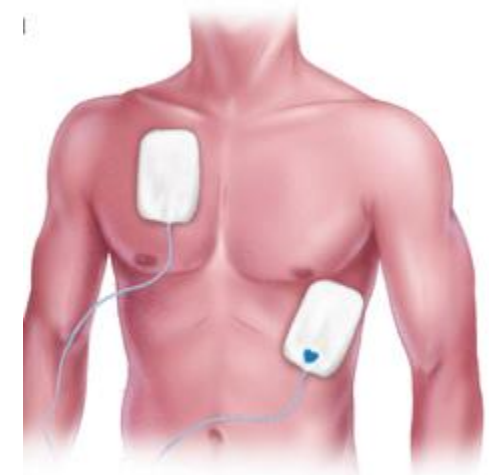
# RISK STRATIFICATION & MITIGATION



# HIGH-RISK MITIGATION STRATEGIES

## Cardiac Overdrive Pacing

- In high-risk cases with severe bradycardia
- Overdrive pacing > 70 bpm can mitigate risk of early-after-depolarizations that can lead to a reentrant rhythm
- All cardiac implanted electronic devices (e.g. pacemakers, ICDs) have capability for overdrive pacing
- Pacing thresholds usually set to HR 40-50 to preserve battery-life and ventricular strain, HOWEVER pacing rates can be increased in high-risk patients
- Alternatively may consider temporary transvenous pacing or “chemical” overdrive pacing with isoproterenol (less common)



## Hemodialysis

- Sudden cardiac death (SCD) is leading cause of death in hemodialysis
- QTc prolongation very common in hemodialysis patients
- Contradicting studies regarding impact of dialysate electrolyte concentrations and serum-to-dialysate gradient measures on QTc
- Goal K<sup>+</sup> in HD patients is 5.1
- **Work closely with nephrology in high-risk patients on HD**





- Do your own QT measurement and HR correction
- “Bazett is Bad” (all other HR correction formulae are fine)
- Correct the QT for a wide QRS – JTc is easy to do!
- 500ms is not an absolute QTc cut-off
- Must consider risk of Torsades vs. benefits of medication in context of patient goals

# QUESTIONS?

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