

Cardiac Event Risk Similar Among Patients on One or Two QT-Prolonging Medications

Team A: Kersten Bartelt, RN; Neil Sandberg

Team B: Matthew Gracianette, MD; Eric Barkley

Last updated 25 September 2025 • Check for updates at EpicResearch.org

Key Findings

- Patients prescribed two concurrent QT-prolonging medications experienced ventricular tachycardia (a type of abnormal heart rhythm) and myocardial infarction at similar rates to patients prescribed only one such medication.
- Cardiac arrest and torsades de pointes (another type of abnormal heart rhythm) were uncommon among patients on one or two medications with a high risk of QT prolongation.

Certain medications can affect the electrical activity of the heart, including lengthening a part of the heartbeat known as the QT interval. This change can increase the risk of dangerous rhythms, such as a rare but potentially fatal condition called torsades de pointes. Many widely used medications, particularly some used to treat heart conditions, infections, and mental health disorders, are known to carry this risk. Current clinical guidelines advise caution when prescribing more than one of these QT-prolonging medications at the same time, especially in patients with underlying heart problems.¹ However, there is limited real-world data quantifying the risk of combining these medications.

We evaluated the rate of serious heart rhythm and cardiac complications among 3,283,463 patients who initiated a new QT-prolonging drug between 2021 and 2024 and had at least one year of follow-up after starting the medication. Patients were categorized based on whether they were prescribed one or two QT-prolonging medications, which were classified as high or low-to-moderate risk.²

Ventricular tachycardia and myocardial infarction were the most common adverse outcomes observed, as shown in Figure 1. Rates were similar for patients prescribed either one or two high-risk medications.

Cardiac arrest, while uncommon, was more frequent among those on one high-risk QT-prolonging drug, occurring in 10.3 per 10,000 patients. Rates of torsades de pointes were very low across all groups regardless of the number of medications prescribed.

Rate of Cardiac Events by Combination of QT-Prolonging Drugs

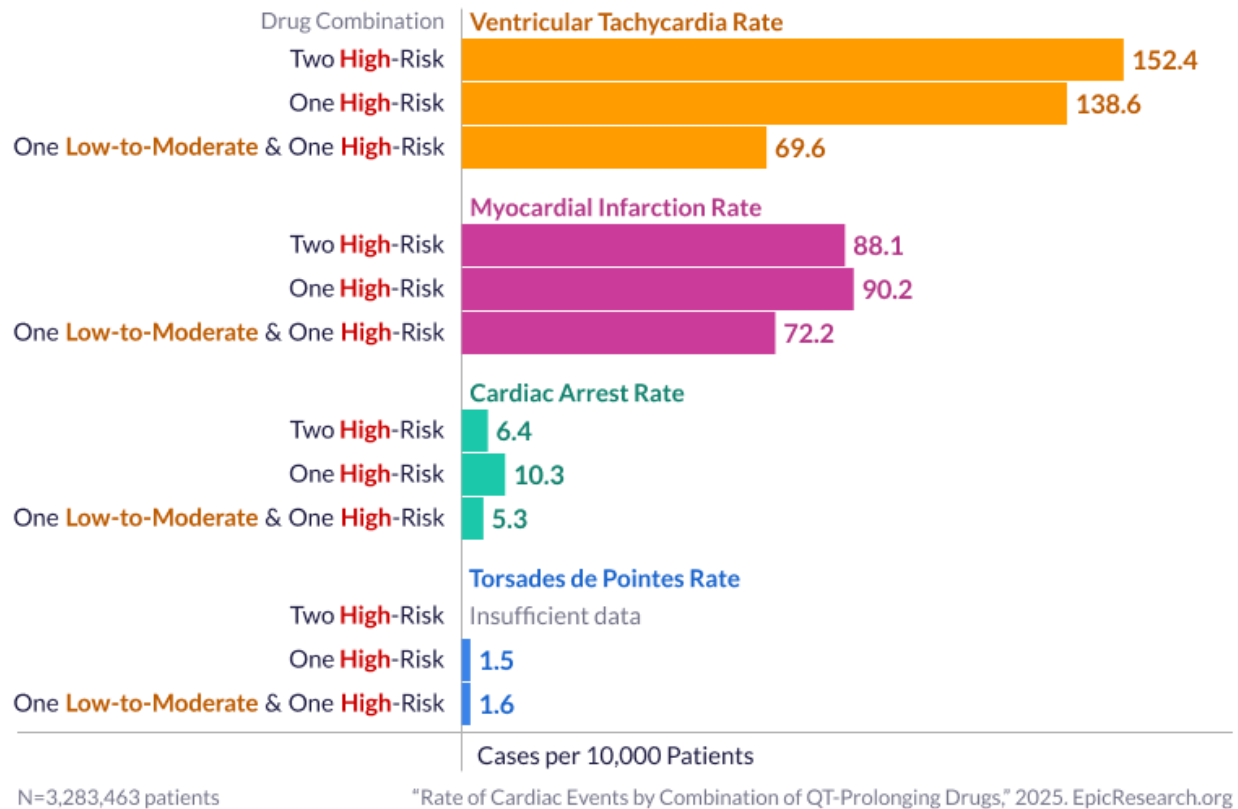


Figure 1. The rate of cardiac events by the combinations of QT-prolonging drugs.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 300 million patient records from 1,800 hospitals and more than 41,000 clinics from all 50 U.S. states, Canada, Lebanon, and Saudi Arabia. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

References

1. Farzam K, Tivakaran VS. QT prolonging drugs. In: StatPearls. StatPearls Publishing; 2025.
2. Berul, C. I. (2024, November 21). Acquired long QT syndrome: Definitions, pathophysiology, and causes. UpToDate. <https://www.uptodate.com/contents/acquired-long-qt-syndrome-definitions-pathophysiology-and-causes>. Accessed March 20, 2025.

Data Definitions

Term	Definition
Study period	2021 to 2024
Study population	Patients prescribed a new QT-prolonging medication during the study period with no changes, such as the medication ending or another QT-prolonging medication starting, over 12 months. Patients must have at least one outpatient care encounter prior to the new prescription and at least one more outpatient care encounter at least 12 months later.
Exposures	The combination of the QT-prolonging medications by risk category. <ul style="list-style-type: none"> A second QT-prolonging medication was included if it overlapped or started concurrently with the first.
Outcomes	Torsades de pointes: ICD-10-CM code I47.21 Other ventricular tachycardia: ICD-10-CM code I47.20 or I47.29 MI: ICD-10-CM code I21*, I22*, or I23* Cardiac arrest: I46*
QT-prolonging medications	<p>High risk was defined as a prescription with a simple generic name of Adagrasib, Ajmaline, Amiodarone, Arsenic trioxide, Astemizole, Bepridil, Bedaquiline, Chlorpromazine, Cisapride, Delamanid, Disopyramide, Dofetilide, Dronedarone, Haloperidol (IM and injection), Ibutilide, Ivosidenib, Lenvatinib, Levoketoconazole, Methadone, Mobocertinib, Procainamide, Quinidine, Quetiapine, Quinine, Revumenib, Selpercatinib, Sertindole, Sotalol, Terfenadine, Vandetanib, Vernakalant, or Ziprasidone</p> <p>Moderate risk was defined as a prescription with a simple generic name of Capecitabine, Carbetocin, Certinib, Chloroquine, Clomipramine, Dabrafenib, Deslurane, Doxifluridine, Encorafenib, Etelcalcetide, Fexinidazole, Floxuridine, Fluorouracil, Flupentixol, Gabobenate dimeglumine, Gepirone, Imipramine, Inotuzumab ozogamacin, Isoflurane, Levetiracetam, Lonafarnib, Meglumine antimoniate, Oxytocin, Pazopanib, Pilsicainide, Piperaquine, Propofol, Quizartinib, Sevoflurane, Sunitinib, Tegafur, or Terbutaline</p> <p>Low risk was defined as a prescription with a simple generic name of Azithromycin, Clarithromycin, Droperidol, Erythromycin, Fluconazole, Haloperidol (non-IV), Levofloxacin, Ondansetron (non-oral), Moxifloxacin, Osimertinib, Pentamidine, Pimozide, Probuco, Propafenone, Ribociclib, Risperidone, Saquinavir, Sparfloxacin, Thioridazine, Toremfene, Vemurafenib, Voriconazole, Olanzapine, Nilotinib, Midostaurin, Lofexidine, Inotuzumab ozogamicin, Halofantrine, Gilteritinib, Gemifloxacin, Gabobenate, Flecainide, Escitalopram, Entrectinib, Doxepin, Domperidone, Dasatinib, Crizotinib, Clozapine, Clofazimine, Citalopram, Chlroquine, Ceritinib, Amisulpride, Albuterol, Alfuzosin, Amitriptyline, Anagrelide, Apomorphine, Arformoterol, Artemether-lumefantrine, Asenapine, Atomoxetine, Benperidol, Bilastine, Bosutinib, Bromperidol, Buprenorphine, Buserelin, Chlorpheniramine, Ciprofloxacin, Clemastine, Cocaine (topical), Degarelix, Desipramine, Desloratadine, Deutetrabenazine, Dexmedetomidine, Diphenhydramine, Dolasetron, Donepezil, Efavirenz, Eliglustat, Eribulin, Etrasimod, Fingolimod, Fluoxetine, Fluphenazine, Fluvoxamine, Formoterol, Foscarnet, Fostemsavir, Gadofosveset, Galantamine, Givinostat, Glasdegib, Goserelin, Granisetron, Hydroxychloroquine, Hydroxyzine, Iloperidone,</p>

	Indacaterol, Itraconazole, Ketoconazole, Lacidipine, Lapatinib, Lefamulin, Leuprolide, Leuprolide-norethindrone, Levalbuterol, Levomepromazine, Levomethadone, Lithium, Loperamide, Lopinavir, Loratadine, Macimorelin, Maprotiline, Mavorixafor, Meclizine, Mefloquine, Mequitazine, Metoclopramide, Metronidazole, Mifepristone, Mirtazapine, Mizolastine, Nelfinavir, Norfloxacin, Nortriptyline, Ofloxacin, Olodaterol, Ondansetron (oral), Osilodrostat, Oxaliplatin, Ozanimod, Pacritinib, Paliperidone, Panobinostat, Paroxetine, Pasireotide, Pefloxacin, Periciazine, Pimavanserin, Pipamperone, Pitolisant, Ponesimod, Primaquine, Promazine, Radotinib, Ranolazine, Relugolix, Rilpivirine, Rivastigmine, Romidepsin, Roxithromycin, Salmeterol, Sertraline, Siponimod, Solifenacin, Sorafenib, Sulpiride, Tacrolimus, Tamoxifen, Telavancin, Teneligliptin, Tetrabenazine, Trazodone, Triclabendazole, Trimeprazine, Triptorelin, Tropisetron, Vardenafil, Vilanterol, Vinflunine, Voclosporin, Vorinostat, or Zuclopenthixol
Outpatient care	Encounters with type "Office Visit," "Well Child," "Follow-Up," "Telemedicine," "Urgent Care," or "Walk-In"

Table 1: Rate of Cardiac Events by Combination of QT-Prolonging Drugs

	MedCount	Value (per 10k)
Ventricular Tachycardia		
Two High -Risk Drugs	4,803	152.4
One High -Risk Drug	79,177	138.6
One Low-or-Moderate & One High -Risk Drug	199,483	69.6
Myocardial Infarction		
Two High -Risk Drugs	4,803	88.1
One High -Risk Drug	79,177	90.2
One Low-or-Moderate & One High -Risk Drug	199,483	72.2
Cardiac Arrest		
Two High -Risk Drugs	4,803	6.4
One High -Risk Drug	79,177	10.3
One Low-or-Moderate & One High -Risk Drug	199,483	5.3
Torsades de Pointes		
Two High -Risk Drugs	4,803	0.0
One High -Risk Drug	79,177	1.5
One Low-or-Moderate & One High -Risk Drug	199,483	1.6