

Use of electrocardiogram monitoring in adult patients taking high-risk QT interval prolonging medicines in clinical practice: systematic review and meta-analysis

**Electronic Supplementary Material 2
Studies Excluded on Full Text**

Drug Safety

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Electronic Supplementary Material 2

Studies Excluded on Full Text

Reasons for exclusion are provided for 74 studies (including 4 studies which could not be located). Studies are presented in order of year published, from most recent.

Berger, F.A., et al., *Comparison of two algorithms to support medication surveillance for drug-drug interactions between QTc-prolonging drugs*. International Journal of Medical Informatics, 2021. **145**: p. 104329.

Reason for exclusion: No relevant ECG use data - ECG use not in relation to (single) high risk drug at follow up.

Dela Cruz, M., M. Ershad, and A. Mostafa, *QTc interval prolongation associated with inpatient azithromycin therapy for pneumonia*. J Am Osteopath Assoc, 2021. **121**(1): p. 5-9.

Reason for exclusion: Could not locate.¹

Soghomonyan, S., et al., *PONV management in patients with QTc prolongation on the EKG*. Frontiers in Pharmacology, 2020. **11**: p. 565704.

Reason for exclusion: No relevant ECG use data.

Monzani, A., et al., *QTc evaluation in COVID-19 patients treated with chloroquine/hydroxychloroquine*. Eur J Clin Invest, 2020. **50**(6): p. e13258.

Reason for exclusion: No relevant ECG use data

Jain, S., et al., *ENHANCED ECG MONITORING OF COVID-19 PATIENTS*. Heart rhythm, 2020.

Reason for exclusion: No relevant ECG use data - ECG use data not in relation to high-risk drugs at baseline / follow-up.

Cruz, M.D., M. Ershad, and A. Mostafa, *QTc Interval Prolongation Associated With Inpatient Azithromycin Therapy for Pneumonia*. The Journal of the American Osteopathic Association, 2020.

Reason for exclusion: Duplicate and previously excluded.

Castro, E., et al., *Should we still monitor QTc duration in frail older patients on low-dose haloperidol? A prospective observational cohort study*. Age & Ageing, 2020. **49**(5): p. 829-836.

Reason for exclusion: ECGs conducted intentionally.

Field, J., et al., *Effect of Chronic Domperidone Use on QT Interval: A Large Single Center Study*. Journal of Clinical Gastroenterology, 2019. **53**(9): p. 648-652.

Reason for exclusion: Baseline and / or follow up ECG do not match protocol definition - Patients included only if baseline ECG and at least one follow up ECG available.

Shao, W., et al., *QTc Prolongation Associated with Psychiatric Medications: A Retrospective Cross-Sectional Study of Adult Inpatients*. Journal of Clinical Psychopharmacology, 2019. **39**(1): p. 72-77.

Reason for exclusion: ECG use data not in relation to initiation of drug therapy or initiation not clearly reported - drugs initiated versus stable treatment not reported; and follow up ECGs not clearly reported; and baseline ECGs conducted intentionally.

Petry, N., et al., *CYP2C19 genotype, physician prescribing pattern, and risk for long QT on serotonin selective reuptake inhibitors*. Pharmacogenomics, 2019. **20**(5): p. 343-351.

¹ Full text could not be sourced online or via the University library.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Ansermot, N., et al., *Prevalence of ECG abnormalities and risk factors for QTc interval prolongation in hospitalized psychiatric patients*. Therapeutic Advances in Psychopharmacology, 2019. **9**.

Reason for exclusion: High risk drugs not studied or drugs do not match protocol definition - ECG data not in relation to high risk drugs and / or baseline and / or follow up.

Daniel, N.M., et al., *Implementation of a QTc-interval monitoring protocol by pharmacists to decrease cardiac risk in at-risk patients in an acute care inpatient psychiatric facility*. Ment Health Clin, 2019. **9**(2): p. 82-87.

Reason for exclusion: ECG use data not in relation to initiation of drug therapy or initiation not clearly reported - ECG data not in relation to initiation of drug; and drugs studied do not match protocol criteria.

Rhew, K., N. Han, and J.M. Oh, *Impact of Safety Warning on Domperidone Prescribing for Geriatric Patients in South Korea: Analysis of National Insurance Claim Data*. Int J Environ Res Public Health, 2019. **16**(16).

Reason for exclusion: ECG use data not in relation to initiation of drug therapy or initiation not clearly reported - drugs initiated versus stable treatment not reported with regard to ECG data; and ECG data combined in one single measure to include both baseline and follow up.

Heemskerk, C.P.M., et al., *Risk factors for QTc interval prolongation*. European Journal of Clinical Pharmacology, 2018. **74**(2): p. 183-191.

Reason for exclusion: High risk drugs not studied or drugs do not match protocol definition - ECG data not in relation to high risk drugs and baseline and / or follow up.

Gerlach, L.B., et al., *Electrocardiogram Monitoring After the Food and Drug Administration Warnings for Citalopram: Unheeded Alerts?* Journal of the American Geriatrics Society, 2018. **66**(8): p. 1562-1566.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Choi, Y., et al., *Risk evaluation of azithromycin-induced QT prolongation in real-world practice*. BioMed Research International, 2018. **2018**: p. 1574806.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Chaudhary, Z. and B. Ramaiah, *Assessment of drug induced QT interval prolongation at a tertiary care, Baptist Hospital, Bangalore*. Pakistan Journal of Medical and Health Sciences, 2018. **12**(4): p. 1871-1874.

Reason for exclusion: High risk drugs not studied or drugs do not match protocol definition - ECG data not in relation to high risk drugs and / or baseline and / or follow up.

Berling, I., et al., *A review of ECG and QT interval measurement use in a public psychiatric inpatient setting*. Australasian Psychiatry, 2018. **26**(1): p. 50-55.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Berger, F., et al., *Media attention regarding sudden cardiac death associated with domperidone use does not affect in hospital ECG recording*. Pharmacoepidemiol Drug Saf, 2017. **26**(11): p. 1418-1424.

Reason for exclusion: ECG data relates not only to adults (includes children).

Vandael, E., et al., *Incidence of Torsade de Pointes in a tertiary hospital population*. International Journal of Cardiology, 2017. **243**: p. 511-515.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Gerlach, L.B., et al., *Unintended Consequences of Adjusting Citalopram Prescriptions Following the 2011 FDA Warning*. American Journal of Geriatric Psychiatry, 2017. **25**(4): p. 407-414.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Bart, G., et al., *Methadone and the QTc Interval: Paucity of Clinically Significant Factors in a Retrospective Cohort*. Journal of Addiction Medicine, 2017. **11**(6): p. 489-493.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Sharma, S., et al., *Providers' Response to Clinical Decision Support for QT Prolonging Drugs*. Journal of Medical Systems, 2017. **41**(10): p. 1-8.

Reason for exclusion: High risk drugs not studied or drugs do not match protocol definition - drugs studied do not match protocol criteria; and ECG data not in relation to baseline and / or follow up

Westermeyer, J., et al., *Long QTc During Methadone Maintenance: Contributors and Interventions Over 4 Years*. J Nerv Ment Dis, 2017. **205**(12): p. 925-930.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Lee, R.A., et al., *Evaluation of baseline corrected QT interval and azithromycin prescriptions in an academic medical center*. Journal of Hospital Medicine, 2016. **11**(1): p. 15-20.

Reason for exclusion: ECG use data not in relation to initiation of drug therapy or initiation not clearly reported - Initiated versus stable treatment not differentiated.

Nicholson, T.T., et al., *Assessing potential risks of treatment with long-term azithromycin in COPD patients: long-term oxygen users beware?* Irish Journal of Medical Science, 2016. **185**(4): p. 993-997.

Reason for exclusion: ECG use data not in relation to initiation of drug therapy or initiation not clearly reported - ECG data not in relation to initiation of high-risk drug and / or baseline and / or follow up.

Niedrig, D., et al., *Drug safety of macrolide and quinolone antibiotics in a tertiary care hospital: administration of interacting co-medication and QT prolongation*. European Journal of Clinical Pharmacology, 2016. **72**(7): p. 859-867.

Reason for exclusion: No relevant ECG use data - ECG use not in relation to (single) high risk drug at baseline.

Dixon, D.L., et al., *Effectiveness of Pharmacist-Led Amiodarone Monitoring Services on Improving Adherence to Amiodarone Monitoring Recommendations: A Systematic Review*. Pharmacotherapy, 2016. **36**(2): p. 230-236.

Reason for exclusion: Qualitative information only; and no relevant ECG use data.

Tricco, A.C., et al., *Interventions to decrease the risk of adverse cardiac events for patients receiving chemotherapy and serotonin (5-HT₃) receptor antagonists: A systematic review*. BMC Pharmacology and Toxicology, 2015. **16**(1): p. 1.

Reason for exclusion: ECG conducted intentionally - ECG performed intentionally in all patients included.

Maljuric, N.M., et al., *Use of selective serotonin re-uptake inhibitors and the heart rate corrected QT interval in a real-life setting: The population-based Rotterdam Study*. British Journal of Clinical Pharmacology, 2015. **80**(4): p. 698-705.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Kram, B.L., S.J. Kram, and K.R. Brooks, *Implications of atypical antipsychotic prescribing in the intensive care unit*. Journal of Critical Care, 2015. **30**(4): p. 814-818.

Reason for exclusion: High risk drugs not studied or drugs do not match protocol definition - high risk drugs not studied.

Calver, L., et al., *The Safety and Effectiveness of Droperidol for Sedation of Acute Behavioral Disturbance in the Emergency Department*. Annals of Emergency Medicine, 2015. **66**(3): p. 230-238.

Reason for exclusion: ECG conducted intentionally - follow up ECG conducted intentionally; and baseline ECG not studied.

Warnier, M.J., et al., *Are ECG monitoring recommendations before prescription of QT-prolonging drugs applied in daily practice? The example of haloperidol*. Pharmacoepidemiology and Drug Safety, 2015. **24**(7): p. 701-708.

Reason for exclusion: Baseline and / or follow up ECG do not match protocol definition - ECG data combined into a single measure for both baseline and follow up and does not match protocol definition.

Vandael, E., et al., *Frequency of use of QT-interval prolonging drugs in psychiatry in Belgium*. International Journal of Clinical Pharmacy, 2014. **36**(4): p. 757-765.

Reason for exclusion: Qualitative information only - qualitative summary of ECG monitoring for QT interval prolonging drugs provided only.

Jardin, C.G., D. Putney, and S. Michaud, *Assessment of drug-induced torsade de pointes risk for hospitalized high-risk patients receiving QT-prolonging agents*. Ann Pharmacother, 2014. **48**(2): p. 196-202.

Reason for exclusion: ECG use data not in relation to initiation of drug therapy or initiation not clearly reported - ECG data not in relation to initiation of high-risk drug.

Tisdale, J.E., et al., *Effectiveness of a clinical decision support system for reducing the risk of qt interval prolongation in hospitalized patients*. Circulation: Cardiovascular Quality and Outcomes, 2014. **7**(3): p. 381-390.

Reason for exclusion: ECG conducted intentionally - all patients underwent baseline ECG (intervention phase) and continuous cardiac telemetry.

Tay, K.Y., M.B. Ewald, and F.T. Bourgeois, *Use of QT-prolonging medications in US emergency departments, 1995-2009*. Pharmacoepidemiology and Drug Safety, 2014. **23**(1): p. 9-17.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Sendelbach, S., et al., *A Computer-Assisted Electrocardiography Measurement Intervention Improves QTc Documentation in Hospital Patients Receiving QT-Prolonging Drugs*. American Journal of Critical Care, 2014. **23**(3): p. e27-8.

Reason for exclusion: Baseline and / or follow up ECG do not match protocol definition - patients excluded from study if ECG not performed.

Price, L.C., et al., *Methadone for pain and the risk of adverse cardiac outcomes*. Journal of Pain and Symptom Management, 2014. **48**(3): p. 333.

Reason for exclusion: Baseline and / or follow up ECG do not match protocol definition - ECG data do not match protocol criteria for baseline / follow up.

Katz, D.F., et al., *QTc interval screening in an opioid treatment program*. American Journal of Cardiology, 2013. **112**(7): p. 1013-1018.

Reason for exclusion: ECGs conducted intentionally.

van den Beuken-van Everdingen, M.H.J., J.W. Geurts, and J. Patijn, *Prolonged QT interval by methadone: relevance for daily practice? A prospective study in patients with cancer and noncancer pain*. Journal of Opioid Management, 2013. **9**(4): p. 263-267.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Tricco, A.C., et al., *Interventions to decrease the risk of adverse cardiac events for post-surgery or chemotherapy patients taking serotonin (5-HT₃) receptor antagonists: protocol for a systematic review and network meta-analysis*. Syst Rev, 2013. **2**: p. 45.

Reason for exclusion: No relevant ECG use data - protocol only of a systematic review.

Thase, M.E., et al., *The cardiovascular safety profile of escitalopram*. European Neuropsychopharmacology, 2013. **23**(11): p. 1391-1400.

Reason for exclusion: ECGs conducted intentionally - baseline and follow up ECG performed intentionally in all patients included.

Patel, N., et al., *Frequency of electrocardiogram testing among HIV-infected patients at risk for medication-induced QTc prolongation*. HIV Med, 2013. **14**(8): p. 463-71.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Pani, P.P., et al., *QTc interval screening for cardiac risk in methadone treatment of opioid dependence*. Cochrane Database of Systematic Reviews, 2013. **2013**(6): p. CD008939.

Reason for exclusion: No relevant ECG use data - no ECG use data.

Linzer, M., et al., *Electrocardiographic abnormalities as potential contributors to premature mortality in patients with mental illness in a psychiatric day treatment program*. Primary Care Companion to the Journal of Clinical Psychiatry, 2013. **15**(3).

Reason for exclusion: No relevant ECG use data - ECG data not in relation to QT-interval prolonging drugs.

Haugaa, K.H., et al., *Institution-wide QT alert system identifies patients with a high risk of mortality*. Mayo Clinic Proceedings, 2013. **88**(4): p. 315-325.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to QT-interval prolonging drugs and / or baseline and / or follow up.

Cunnington, A.L., K. Hood, and L. White, *Outcomes of screening Parkinson's patients for QTc prolongation*. *Parkinsonism and Related Disorders*, 2013. **19**(11): p. 1000-1003.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Beysens, M., *Quel suivi cardiométabolique des patients traités par antipsychotiques ? (enquête auprès des généralistes et des psychiatres du Poitou-Charentes)*. Thesis in French. 2012, University of Poitiers, France. 1 vol., p. 155

Reason for exclusion: Could not locate.²

Tisdale, J.E., et al., *Prevalence of QT interval prolongation in patients admitted to cardiac care units and frequency of subsequent administration of QT interval-prolonging drugs: a prospective, observational study in a large urban academic medical center in the US*. *Drug Safety*, 2012. **35**(6): p. 459-470.

Reason for exclusion: ECGs conducted intentionally - all patients underwent continuous cardiac telemetry and / or baseline ECG.

Miranda, D.G., C.L. McCain, and A.J. Smith, *Medication-induced QT-interval prolongation and torsades de pointes*. *U.S. Pharmacist*, 2011. **36**(2): p. HS2-HS8.

Reason for exclusion: Could not locate.³

Mayet, S., et al., *Methadone maintenance, QTc and torsade de pointes: Who needs an electrocardiogram and what is the prevalence of QTc prolongation?* *Drug and Alcohol Review*, 2011. **30**(4): p. 388-396.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Mabasa, V.H., et al., *Analysis of orders for QTc-prolonging medication for intensive and cardiac care unit patients with pre-existing QTc prolongation (QTIPPP study)*. *Canadian Journal of Hospital Pharmacy*, 2011. **64**(6): p. 412-418.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

McNamara, J.K., et al., *Methadone-associated prolongation of the QTc interval at doses used for chronic pain*. *P and T*, 2011. **36**(2): p. 78-107.

Reason for exclusion: ECG use data not in relation to initiation of drug therapy or initiation not clearly reported - drug initiated versus stable treatment not reported; and insufficient information; and post-initiation ECGs not clearly defined.

Methadone-Associated Prolongation of the QTc Interval at Doses Used for Chronic Pain. 2011, MediMedia Managed Markets, an ICON Company. p. 78-107.

Reason for exclusion: Duplicate and previously excluded.

Lallemant, B.M.H., *Contribution of ECG and interest of the analysis of repolarisation (QT interval) by the general practitioner during the prescription of psychoactive drug (From a case control study of 50 patients)*. Thesis in French. 2010, Aix Marseille University, France. 1 vol., p. 96

² Full text could not be sourced online or via the University library

³ Full text could not be sourced online or via the University library

Reason for exclusion: Could not locate.⁴

Pickham, D.M., *Prevalence of and predictors for QT interval prolongation and adverse outcomes in an acutely ill cohort: the QTIP Study*. 2010, University of California, San Francisco. p. 184 p-184 p.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to QT-interval prolonging drugs and / or baseline and / or follow up.

Pickham, D., et al., *How many patients need QT interval monitoring in critical care units? Preliminary report of the QT in Practice study*. J Electrocardiol, 2010. **43**(6): p. 572-6.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to QT-interval prolonging drugs and / or baseline and / or follow up.

Ghosh, S., et al., *Monitoring electrocardiograms of service users on high-dose methadone substitution therapy: An audit*. Psychiatrist, 2010. **34**(11): p. 489-491.

Reason for exclusion: ECG use data not in relation to initiation of drug therapy or initiation not clearly reported - ECG data not in relation to initiation of high-risk drug.

Fareed, A., et al., *Onsite QTc interval screening for patients in methadone maintenance treatment*. J Addict Dis, 2010. **29**(1): p. 15-22.

Reason for exclusion: ECG use data not in relation to initiation of drug therapy or initiation not clearly reported - ECG data not in relation to initiation of high-risk drug.

Reddy, S., et al., *The effect of oral methadone on the QTc interval in advanced cancer patients: a prospective pilot study*. J Palliat Med, 2010. **13**(1): p. 33-8.

Reason for exclusion: ECGs conducted intentionally - ECG conducted with intention at baseline and follow up.

Weidman-Evans, E., et al., *Impact of a pharmacist developed protocol on the cardiac monitoring of methadone in chronic noncancer pain management*. J Am Pharm Assoc (2003), 2009: p. e102-e109.

Reason for exclusion: No relevant ECG use data - ECG use not in relation to baseline and / or follow up.

Darwiche, F.Z., S.T. Ugradar, and T. Turner, *Junior doctors' knowledge and practice of electrocardiographic monitoring for high-risk patients receiving antipsychotic medications*. Psychiatric Bulletin, 2009. **33**(10): p. 377-380.

Reason for exclusion: High risk drugs not studied or drugs do not match protocol definition - drugs studied do not match protocol criteria.

Snider, M., S. Kalbfleisch, and C.A. Carnes, *Initial experience with antiarrhythmic medication monitoring by clinical pharmacists in an outpatient setting: a retrospective review*. Clinical Therapeutics, 2009. **31**(6): p. 1209-1218.

Reason for exclusion: ECG use data not in relation to initiation of drug therapy or initiation not clearly reported - drugs initiated versus stable treatment not reported.

Van Der Sijs, H., et al., *Clinically relevant QTc prolongation due to overridden drug-drug interaction alerts: A retrospective cohort study*. British Journal of Clinical Pharmacology, 2009. **67**(3): p. 347-354.

Reason for exclusion: No relevant ECG use data - ECG use not in relation to (single) high risk drug at baseline and / or follow up.

⁴ Full text could not be sourced online or via the University library

Van Der Sijs, H., et al., *Unintended consequences of reducing QT-alert overload in a computerized physician order entry system*. European Journal of Clinical Pharmacology, 2009. **65**(9): p. 919-925.

Reason for exclusion: No relevant ECG use data – study subjects excluded if no ECG before and within 1 month (of alert override).

Frimas, V., et al., *[Cardiological monitoring of antipsychotic-treated patients: evaluation and evolution of a hospital protocol]*. [Article in French]. Encephale, 2008. **34**(5): p. 467-76.

Reason for exclusion: ECG use data not in relation to initiation of drug therapy or initiation not clearly reported - ECG data not in relation to initiation of high-risk drug.

Ng, T.M.H., et al., *Pharmacist monitoring of QTc interval-prolonging medications in critically ill medical patients: A pilot study*. Annals of Pharmacotherapy, 2008. **42**(4): p. 475-482.

Reason for exclusion: ECGs conducted intentionally - ECGs routinely ordered on ICU admission; and patients without follow up ECGs excluded.

Nuttall, G.A., et al., *Does low-dose droperidol administration increase the risk of drug-induced QT prolongation and torsade de pointes in the general surgical population?* Anesthesiology, 2007. **107**(4): p. 531-6.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Golzari, H., et al., *Prolonged QTc intervals on admission electrocardiograms: Prevalence and correspondence with admission electrolyte abnormalities*. Connecticut Medicine, 2007. **71**(7): p. 389-397.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to QT-interval prolonging drugs and / or baseline and / or follow up.

Moosa, M.Y.H., F.Y. Jeenah, and C. Mouton, *ECG changes in patients on chronic psychotropic medication*. South African Journal of Psychiatry, 2006. **12**(3): p. 42-46.

Reason for exclusion: ECG use data not in relation to initiation of drug therapy or initiation not clearly reported - ECG data not in relation to initiation of high-risk drug

Benoit, S.R., et al., *Risk factors for prolonged QTc among US adults: Third National Health and Nutrition Examination Survey*. European Journal of Cardiovascular Prevention and Rehabilitation, 2005. **12**(4): p. 363-368.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Lin, C.H., et al., *Predictive factors for QTc prolongation in schizophrenic patients taking antipsychotics*. Journal of the Formosan Medical Association, 2004. **103**(6): p. 437-441.

Reason for exclusion: No relevant ECG use data - ECG data not in relation to baseline and / or follow up.

Unnikrishnan, D., et al., *Cardiac monitoring of patients receiving arsenic trioxide therapy*. British Journal of Haematology, 2004. **124**(5): p. 610-617.

Reason for exclusion: No relevant ECG use data - No ECG use data (in the observational cohort).