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Letter to the editor

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**HEROIN ADDICTION &  
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## QTc Interval Screening. American Association for the Treatment of Opioid Dependence (AATOD) Policy and Guidance Statement

Mark Parrino and AATOD Board of Directors

*American Association for the Treatment of Opioid Dependence*

TO THE EDITOR: Opioid Treatment Programs (OTPs) should be responsible and vigilant about assessing for the risk of cardiac conduction disturbance in methadone maintained patients and policies should be guided by the evidence of risk for QTc prolongation and Torsade de Pointes (TdP). The threshold for determining guidelines for screening and monitoring must be balanced with the potential barriers to treatment access and the financial burden that routine screening places on patients and programs. AATOD takes the risk for QTc prolongation and TdP in methadone treated patients very seriously. While the literature argues for and against routine testing prior to admission to an OTP, the evidence does not justify routine electrocardiographic (ECG) screening for all methadone treatment patients and does not conclude at which dose level patient should obtain ECG screening [4, 14]. The recommendations below represent our best guidance informed by more than 40 years of methadone treatment experience and the research to date.

Laboratory studies [9, 20] and case reports [2, 6, 10, 11, 17, 19, 22] suggest that methadone, whether prescribed for pain or addiction, has the potential for cardiac arrhythmia complications specifically QT-prolongation and TdP. Methadone alone, however, did not account for the majority of these complications. Contributing factors include pre-existing cardiac disorders, i.e. cardiomyopathy, genetic predisposition, hypokalemia, and taking multiple drugs of abuse or other medications known to prolong QT interval [8, 12, 21]. Studies that examine methadone dose and QTc prolongation have mixed results [13-15, 17, 19, 22]. Opinions about management of this potential

risk vary from aggressive intervention including ECG prior to administering any QTc prolonging medications [7, 15], to screening only patients on "high" doses of methadone, although there is no clarity what defines a high dose level [1, 16, 18, 22]. Others recommend only screening high-risk patients [3, 7, 11].

After a review of the evidence-based research, CSAT consensus panel draft recommendations and our experience, AATOD recommends the following for the assessment of cardiac conduction risk in methadone treatment patients:

1. Physicians and other medical staff working in OTPs and Pain Management programs should be educated about the risk of QTc/TdP in methadone maintained patients.
2. OTPs and Pain Management programs should develop a Comprehensive Cardiac Arrhythmia Risk Management Plan that includes the type, threshold and frequency for screening and monitoring. The plan should include a review of:
  - A personal medical history of long QT syndrome, cardiac conduction defects, arrhythmias, syncope episodes, seizures, palpitations, dizziness and lightheadedness, and a family history of long QT syndrome, cardiac conduction defects, arrhythmias, syncope episodes, seizures and sudden or unexpected death should be part of a medical assessment prior to admission to an OTP.
  - Electrolytes disturbances, in particular hypokale-

Correspondence: Mark Parrino, MS. American Association for the Treatment of Opioid Dependence (AATOD) - 225 Varick Street, 4th Floor; New York, NY 10014, USA - Phone 212 566 5555 Fax 212 366 4647 - Email: info@aatod.org

mia and hypomagnesemia and medications that can induce these conditions (diuretics and laxatives) should be included in the medical assessment.

- The assessment should note any history of clinically significant bradycardia or other relevant cardiac disease.
  - A review of all prescribed medications prior to induction onto methadone treatment with particular attention paid to those medications that are substrates of CYP3A4/CYP2D6, CYP2B6 and those that block HERG channel currents. New medications including over-the-counter (OTC) agents, herbal preparations, and dietary supplements should be reviewed with the program physician. ([www.Torsade.org](http://www.Torsade.org))
  - A review of toxicology screens for the presence of illicit drugs particularly cocaine and amphetamines.
3. Medically frail patients, patients prescribed additional opioids for chronic pain management and patients with a history of poor, extensive or rapid metabolism of methadone should be closely monitored.
  4. Consent to methadone treatment should include information about the risk of using illicit drugs particularly drugs diluted with quinine.

AATOD recommends the following for management of cardiac conduction risk in methadone maintained patients:

1. Consider a baseline and follow-up 12-lead ECG for patients with "a history of arrhythmia, prolonged QTc, a family history of premature death, and/or other significant arrhythmia risk factors" on admission or for suspected arrhythmia risks in ongoing methadone maintained patients [14].
2. Referral should be made for cardiac consultation for "known or detected cardiac conditions affecting heart rhythm, unexplained syncope or seizures or a significant increase in QTc from the baseline if known [14].
3. Patients at-risk should be educated on cardiac symptoms to watch for e.g. "racing" heartbeat, dizziness, seizures, or fainting spells and encouraged to contact the clinic" and medical provider and/or emergency services immediately [14].

AATOD believes that the safeguards outlined above along with individualized induction practices will allow clinicians to optimize safety during methadone treatment [5]. Informed and appropriate clinical monitoring and follow-up will be the best protection for patient safety. Prospective clinical trials are needed before routine ECG screening can be endorsed.

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