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► [Onsite QTc interval screening for patients in methadone maintenance treatment.](#)



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*Does the small risk of fatal heart attack potentially posed by methadone justify routine electrocardiogram screening of patients, or will this cause more deaths by limiting an effective treatment for opiate addiction? A US clinic tried it and found three at-risk patients in three years.*

**Summary** The QTc interval is an indicator of heart function derived from electrocardiogram measures. It refers to the delay between two phases of the electrical activity of the heart which drives it in pumping blood round the body. Extended intervals may lead to torsades de pointes, a potentially life threatening heart attack. Several studies have reported that methadone may contribute to the elongation of this interval, heightening the risk. The risk threshold has been variously set at 450ms (0.45 seconds) for men and 470ms for women or 450ms for both, though it is generally accepted that intervals greater than 500ms constitute a significant risk of abnormal heart function.

Given the risk, an expert US panel [recommended](#) electrocardiogram screening of all methadone patients when they start treatment and then a month and a year later, with extra tests as indicated.

A medical clinic for former US military personnel instigated such screening at the clinic itself to identify high risk patients. Alongside it offered brief on-site counselling for patients about the risks of cardiac arrhythmias associated with methadone and how to spot the symptoms of any impending problems. Electrocardiogram results were reviewed by the clinic's psychiatrist, who provided feedback for each patient and arranged for appropriate referrals as needed. Patients with automated readings between 450ms and 500ms received more education and further electrocardiogram monitoring. If the interval reading exceeded 500ms, methadone dose was reduced and the patient was referred to a cardiology clinic.

The featured article reports on the feasibility and effectiveness of these procedures instigated in 2007 based on the records of 55 patients treated between 2002 and 2009 who were among the clinic's established caseload and had been retained in methadone treatment for at least six months and not dropped out. These patients averaged 90mg methadone daily.

## Main findings

Urine drug screens revealed that illicit opiate and cocaine use fell during treatment, until just 4–5% of the latest tests were positive for each drug. All but 5% of patients underwent electrocardiogram screening as intended at admission and annually. At baseline the QTc interval averaged 417ms but increased to 442ms at the latest test, a statistically significant prolongation. Two thirds of the patients registered a significant prolongation but remained below 450ms. Another 27% ended up between 450ms and 500ms while just 6% experienced a statistically significant QTc prolongation which ended by exceeding 500ms. No patient was required as a result to discontinue methadone.

Statistical tests were used to determine whether QTc prolongation was significantly related to methadone dose, duration in treatment, whether the patient smoked, concomitant use of antidepressants and antipsychotics, or cocaine use either at baseline or recently. Of these, only recent cocaine use was significantly related to QTc prolongation, both when each variable was tested one by one and when all were taken in to account at the same time.

## The authors' conclusions

This study confirms that methadone is a safe and effective treatment for opiate dependence. Although other factors such as continued illicit drug use, hepatitis C, HIV and smoking are much more likely to lead to premature death in methadone patients than cardiac arrhythmias, QTc prolongation in addition to other chronic medical conditions may increase the risk. An electrocardiogram is an objective tool to identify patients at risk for cardiac arrhythmias. Although such screening itself is not expensive, referral to specialty care could be, but in practice providing on-site electrocardiogram screening with a focus on patient education and limiting referral to cardiology specialty care led over a three-year period to just three of 55 patients being referred.

Two thirds of retained patients in the clinic had QTc intervals within the normal range and only three of 55 exhibited significantly increased risk for torsades de pointes with a QTc of over 500ms. Interventions initiated by the addictions clinic included methadone dose reduction, elimination or reduction of other QTc-prolonging medications, education about the possible contributions of caffeine and nicotine to QTc prolongation, and detailed information about the signs and symptoms of arrhythmias.

The key finding in this study was that recent but not baseline use of cocaine among methadone patients – meaning that even when established in treatment these patients had continued with its use – was associated with QTc prolongation.

 Whether the so far largely theoretical and circumstantial risk of death from torsades de pointes due to methadone's effects justifies routine and repeated electrocardiogram screening of all patients is a matter of some contention. The expert panel convened by the US government whose initial recommendations prompted the

featured study later [changed its mind](#), due largely to concern that this might on balance cause more deaths by limiting an effective treatment for opiate addiction. It could mean delays as patients await electrocardiogram testing and results, divert resources from methadone treatment, lead some patients to reject or drop out of methadone treatment, or to sub-optimal doses, all of which could lead to preventable deaths. Faced with these risks the panel opted for screening high risk patients only. However, this could mean still having to screen most patients, as a UK study [demonstrated](#).

In line with the featured study's findings, the [latest report](#) of the US expert panel noted that cocaine use seems to aggravate any impact of methadone on the QT interval. [Laboratory studies](#) have shown that in its own right cocaine has a marked impact on the QT interval. Such findings justify including use of the drug among the variables indicating high risk among methadone patients, [one of the reasons](#) why in parts of Britain so many would qualify for this designation.

High methadone doses are thought to heighten the cardiac risk but also protect against potentially fatal illicit opiate use. In this respect it would have been useful if the featured report had been able to record the consequences of the cautionary dose reductions it implemented among the sampled patients, especially whether urine screens indicated increased illicit drug use after methadone was reduced. Also of interest is whether these or other initiatives implemented as part of the described programme led any patients to refuse or drop out of treatment (in which case they would not have been among the sample reported on), or to be offered or insist on a lower than optimal dose.

See this [Findings analysis](#) of the US panel's latest report for more on the risk of death due to methadone-provoked QT prolongation, on whether universal electrocardiogram screening is advisable given the size of this risk and the possible unintended consequences of requiring such screening, and on UK guidance.

*Thanks for their comments on this entry in draft to Ayman Fareed of the Atlanta Veterans' Affairs medical service and Emory University School of Medicine in the USA. Commentators bear no responsibility for the text including the interpretations and any remaining errors.*

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