



Evaluating the Risk of Methadone and QTc Interval Prolongation in an Oncologic Population

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Background

- Methadone is commonly used as an alternative to other opioids for managing cancer-related pain [1,2]
- High-dose methadone (>100 mg/day), primarily in opioid dependence treatment, has been associated with QTc prolongation [3]
- The cardiovascular effects of methadone at lower doses, as used in cancer pain management, remains less well characterized

Objectives

- Primary objective: To determine the prevalence of QTc prolongation (>450 ms in males, >470 ms in females) in cancer patients treated with methadone for pain
- Secondary objective: To identify clinical risk factors and co-administered medications associated with QTc prolongation

Methods

- Retrospective analysis of 492 adult patients receiving methadone for cancer pain management
- Collected the following demographic and clinical data: age, sex, cancer diagnosis, methadone dosage, adjuvant medications, comorbidities
- Extracted QTc interval measurements from ECGs prior to methadone initiation, 0-6 months after, 6-12 months after, and >12 months after

Results

Timepoint	ECG Data (n)	Normal QTc (n)	Prolonged QTc (n)	Normal QTc (%)	Prolonged QTc (%)
Baseline	492	477	15	97	3
0-6 months	391	373	18	95.4	4.6
6-12 months	184	174	10	94.6	5.4
12+ months	207	193	14	93.2	6.8

Table 1. Mean QTc intervals at different timepoints calculated using the Fridericia correction (QTcF)

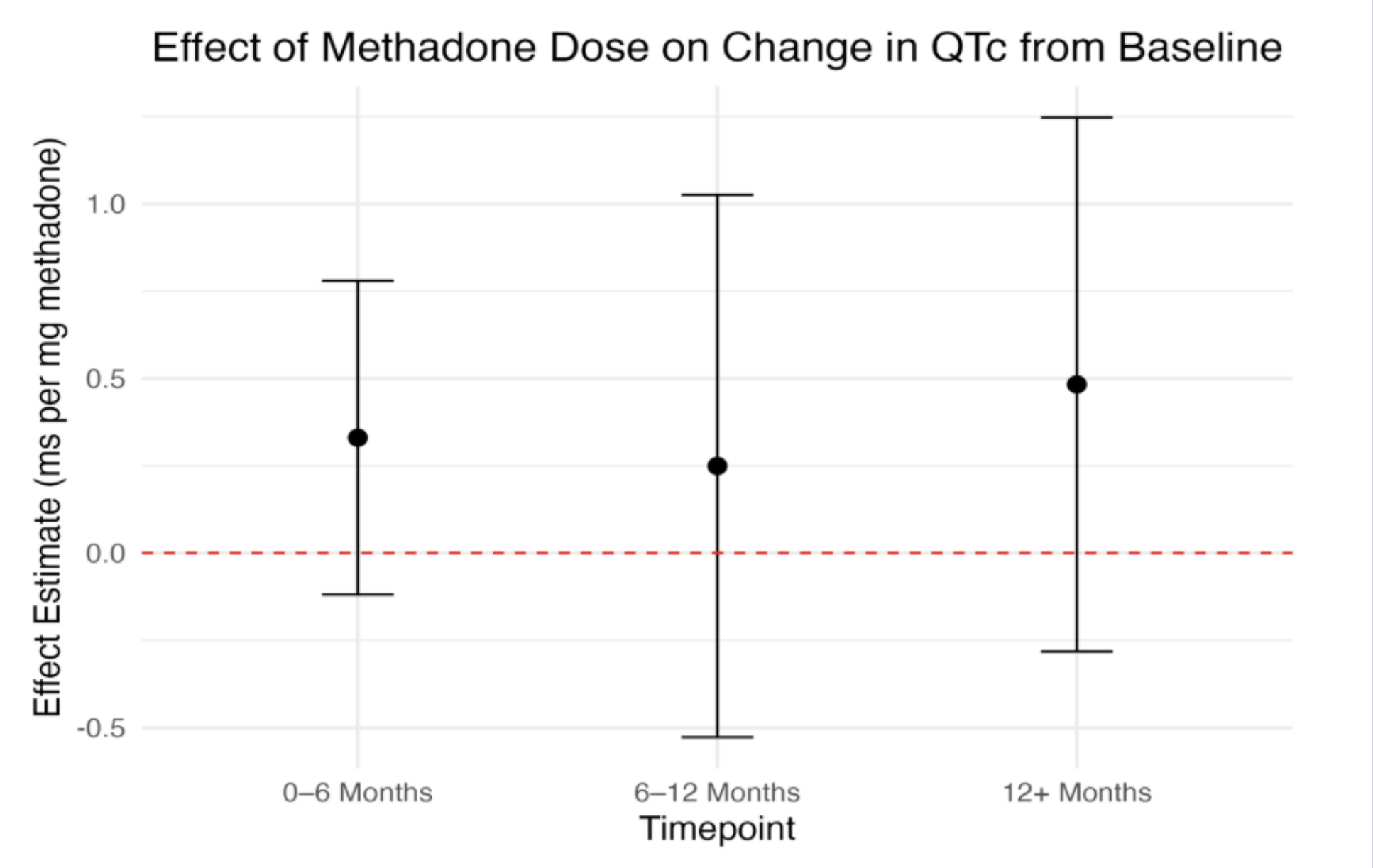


Figure 1. Estimated change in QTc interval relative to baseline (in milliseconds) per 1 mg increase in daily methadone dose

Table 1 and Figure 1:

- The proportion of patients with prolonged QTc increases modestly from 3% at baseline to 6.8% at 12+ months after methadone initiation
- Majority of patients (>93%) maintain normal QTc interval 12+ months after methadone initiation
- No statistically significant association between daily methadone dose and change in QTc interval ($p > 0.05$ for all timepoints)

Variable	Timepoint	Effect Size on QTc (ms)	P-value
Gabapentinoids	0-6 months	-8.86	0.001
Antidepressants	0-6 months	+6.46	0.032
Electrolyte Abnormalities	0-6 months	-8.78	0.012
Antidepressants	6-12 months	+13.69	0.002

Table 2. Variables associated with changes in QTcF from baseline (multivariable regression analysis)

Table 2:

- Several adjuvant medications were associated with changes in QTc from baseline

Discussion

- No significant association between daily methadone dose and QTc prolongation, reinforcing the overall cardiac safety of methadone in lower doses for cancer pain management
- Adjuvant medications (antidepressants in particular) showed significant associations with a prolonged QTc, consistent with evidence that these medications blockade potassium channels, which underscores the risk of polypharmacy in patients taking methadone
- Limitations include the retrospective design, potential confounding, and missing ECG data at later timepoints

Conclusion

- Lower doses of methadone used for cancer pain management do not result in significant levels of QTc prolongation over time
- These findings emphasize the importance of monitoring for cardiac effects in patients on more complicated medication regimens, even when methadone is used at lower doses

References:

