

Review of: "Methadone In Chronic Non-Oncological Pain: From Disassuefaction Of Painkillers Abuse To The Primary Management Of Opioid Hyperalgesia"

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Potential competing interests: The author once had a small amount of stocks of the respirator/ventilator company Draeger in his private portfolio

This is an interesting review focusing on the potential of methadone. The authors not only address the advantages as a painkiller in chronic pain and disassuefaction of painkiller-abuse, but also the dangers (e.g. interaction with other drugs, risk for accumulation due to long half life, and the prolongation of the QTc interval). To improve the manuscript further, I have the following suggestions:

1. Style: I would suggest to have the paper proofread by a professional, native-speaking proofreader. Although the manuscript is mostly well-written, there are some grammar mistakes. In addition, a comma is once mixed up with an end of sentence marker and a sentence is once interrupted in the middle.
2. Content: The authors briefly relate to neuropathic pain, but they never discuss alternative medication such as pregabalin and gabapentin. A short passage with a focus on these would make sense.
3. Dangers: When dealing with the danger of QTc prolongation, it is true that an ECG prior to starting methadone is mandatory, but an ECG following the start of methadone is also mandatory, because one needs to find out what effect methadone has on the patient's QTc interval. This is important as one wants to avoid the risk of Torsades de pointes. This has not been addressed in their review yet. The authors write one should refrain from using methadone if QTc prior to its start is 500 ms or longer. However, it may already become dangerous if QTc is shorter than 500 ms initially because methadone carries the risk of accumulation. Therefore, ECGs should be repeated in the course of treatment.