Reviewer’s report

Title: The Effectiveness of Opioid Substitution Treatments for Patients With Opioid Dependence: A Systematic Review and Multiple Treatment Comparison Protocol

Version: 1

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Reviewer: Laxmaiah Manchikanti

Reviewer’s report:

The authors have prepared a protocol for a systematic review comparing multiple treatments for opioid dependence. The subject is worthwhile for discussion.

The study design is appropriate.

The authors have provided seemingly sufficient details to allow replication of work or comparison with related analysis. However, the authors seem to have used old references and the data which is not very clear. The authors do mention that reported methadone effectiveness varies by studies, with some investigations reporting as low as 20% to as high as 70%. One of the references by Dressler and Roberts is a 1989 reference and it analyzed only 80 cases at necropsy. The reference by Dutta appears to be related to HIV. Reference 12 by Birnbaum is also not an original article describing these issues. Finally, reference 13 is not a reference which the reader can look at.

Most importantly, the authors should consider toxic effects of methadone and emerging abuses of Suboxone. Both methadone, as well as Suboxone, are available freely to anyone who has money. Generally it is stated that in specifically smaller areas, what all they need to do is go and take one hydrocodone or something to that effect. They will be tested positive for hydrocodone and they will be considered as drug abusers. Consequently, they put them on high doses of methadone. As a practitioner of 30 years in pain medicine, I have not seen a single patient who has been off drugs after methadone treatment. Further, the U.S. FDA has recommended a dose of 30 mg per day. Methadone clinics do not meet these recommendations. Suboxone, the new emerging drug of abuse, is functioning as a moneymaker for many clinics. There is no significant data in reference to their efficacy in detoxifying. I have seen hundreds and thousands of patients who have been to Suboxone and methadone clinics seeking the same drug or stronger drugs again. However, this is considered as anecdotal experience even though the majority of physicians have agreed with this information. There are significant lobbying groups supporting these clinics. Consequently, the truth may never come out in the appropriate literature. However, this should not discourage the authors to perform this systematic review. The best way to do this is to get the most appropriate literature and all sides to be incorporated in this analysis.
The planned statistical analysis appears to be appropriate.
The writing is also acceptable.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.