Reviewer's report

Title: Pharmacotherapy for Bipolar Disorder and concordance with treatment guideline: a tertiary care survey.

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Reviewer: Mark Bauer

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The authors present an interesting descriptive study of individuals with bipolar disorder referred to a tertiary care clinic. They find relatively high rates of concordance with CANMAT guidelines and identify hypomania and bipolar II disorder as predictors of lower concordance. This descriptive study could be informative, although clarification is needed especially in the Methods.

Major Issues:

While this appears to be a straightforward descriptive study at first reading, there are several issues around defining guideline concordance.

• CANMAT guidelines are quite lengthy and have many components or choice-nodes (as is the case with most guidelines). How were the “nodes” or criteria specifically chosen by which individuals were classified guideline-concordant or not? Was this done a priori?

• p9, para 1 contains the meat of the classification scheme. Are we to understand that prescriptions for the classes of medications listed on line 1 in any dose were sufficient for classification as guideline adherent? Is this truly what CANMAT says—any dose is good enough? Perhaps this is why the reported adherence rates are higher than other studies (p 14 last line). It would be more informative to report based on therapeutic doses or serum levels where relevant.

• In p9 para 2, it appears that those “receiving prescribed treatment not included in the CANMAT recommendations” are classified as “doesn’t follow the guidelines.” What about individuals with comorbidity? If a person receives a stimulant for comorbid ADHD, does this make them non-concordant? Apparently so (Table 4 footnote). Similarly, subtherapeutic doses of lithium apparently qualify as guideline-concordant, while subtherapeutic doses of trazodone make them non-concordant (again, Table 2, footnote). Further, how were benzodiazepines for anxiety handled? They are likely not included in CANMAT (for bipolar disorder) but may be used for anxiety disorders. In summary the classification scheme remains (a) unclear and (b) possibly problematic.

• Similarly, several of the anticonvulsants listed in Table 2 are not widely considered efficacious in bipolar disorder—gabapentin, topiramate, leviteracetam. Are these truly CANMAT-endorsed?

• The authors take some pains to differentiate first- from second- from third-line treatment. What these consist of is not clear to the reader. It would be curious,
for example, if subtherapeutic doses of leviteracitam qualified for guideline-concordance by virtue of being a third-line treatment. The authors should make a decision, and justify it explicitly, as to why third-line and second-line treatments are included as guideline-concordant (the latter is an easier justification to make, particularly in referrals to a tertiary care clinic, than the former).

- It appears that for some purposes polypharmacy is considered guideline-concordant (p9) and sometimes not (Table 4).
- For both first/second/third-line treatments and for polypharmacy, it should be made clear which are the primary vs. secondary analyses.

Additional Issues:
- Though the title refers to “tertiary care” survey, the data really reflect community practice since they assess treatment upon referral. This should be clarified—and in fact studying community practice makes it more interesting than studying tertiary care.
- The authors note that 20% of referrals were accepted (p7 para 2). What happened to the other 80%?
- The ROMHC acronym appears in the abstract and should be written out or handled some other way than just the acronym.
- In p9 para 2, “…though in associations not…” should be “combinations.”
- On page 15 para 1 in discussing bipolar type II as a predictor of non-concordance, it is worth mentioning that this is (or appears to be the case) in several studies summarized in Table 1
- Table 3 is inconsistent in footnoting: NS gets a dagger sometimes, but many rows are blank (presumably NS). Dagger not needed.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**
'I declare that I have no competing interests’