Reviewer's report

Title: Skating on thin ice: pragmatic prescribing for treatment refractory schizophrenia

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Reviewer: Joseph M Pierre

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Overall, an interesting and valuable paper looking at naturalistic use of antipsychotic treatment on an inpatient ward that focuses on treatment refractory patients and evidence-based practice. The major weaknesses of the paper -- the lack of randomization and controls and the retrospective ratings of psychopathology -- are well acknowledged by the authors, and as they argue, these same weaknesses offer the potential benefit of examining outcomes in a more "real world" fashion. In fact, the results confirm treatment recommendations based on RCT evidence, emphasizing the utility of clozapine as well potential benefits of dose reductions and avoidance of polypharmacy. It is valuable to see support of those practices in more naturalistic settings.

Major Compulsory Revisions

1. Given lack of randomization, the major limitation of the study is that it leaves unanswered the question of whether the apparent advantages of certain treatment strategies were dictated by the interventions vs. disease states that governed the choice of intervention. It would therefore be useful, at the very least, to tabulate differences in patient demographics (e.g. age or sex) and diagnosis (co-morbid substance abuse, axis II) according to different treatment strategies. That kind of demographic data is expected in a controlled trial, and is all the more important here.

   It would be helpful to know whether such factors were predictive of different treatment strategies, and whether the factors themselves might have contributed to outcome (e.g. was there, as might be expected, a more favorable course with female patients?). Ideally, the potential contribution of such factors -- e.g. age, sex, diagnosis -- should be explored statistically.

2. Along these lines, the absence of schizoaffective disorder is striking here, particularly given the high rate of "mood stabilizer" prescribing. Were there really no patients who met criteria for schizoaffective disorder? Some would argue that patients with schizoaffective disorder have a more favorable clinical course or that they might preferentially respond to anticonvulsant augmentation. The authors should clarify whether -- or why -- no schizoaffective disorder was present (e.g. were they excluded from the study?).

Minor Essential Revisions
3. As a reviewer in the US, I am unclear on the authors' use of the word "rationalise" in the context of medication and dosing. Do the authors mean rationing? Or dosing based on evidence in a rational fashion? Either way, I would suggest using a different word.

4. I am curious about the comorbidity of axis II pathology comorbid to schizophrenia. It would be useful to specify which personality disorders were co-occurring.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests