Reviewer's report

Title: Adjusting for Geographic Variation in Observational Comparative Effectiveness Studies: A Case Study of Antipsychotics Using State Medicaid Data

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Reviewer: Yunjie Song

Reviewer's report:

1. The question is not well-defined. In the background of the abstract, authors state that variation is a potential source of bias in comparative effectiveness studies and ESDA and spatial statistics can control the bias. Variation in outcomes can be biased because of various reasons, but it is not a source of bias. As the authors show, it is incomplete controls that cause bias. Spatial techniques do work well to remove the bias, but in the paper it is the multivariable logistic regressions that strongly support authors’ arguments – when more covariates are controlled, ORs are no more significant. The logistic regressions appear not dependent on spatial statistics.

2. The authors described the methods well. One of minor issues can be a lack of numbers of counties or HMSAs over there.

3. The data are not quite sound. As the authors pointed out, the case of aliperidone palmitate users is too small. More critically, aliperidone palmitate users are far different from SGA users. For example, ages are 37 vs 26, blacks are 42% vs 19%, Schizophrenia and other psychotic disorders are 82% vs 12%, and 3 or more conditions are 65% vs 38%. It appears that the psychotic problems faced by aliperidone palmitate users are far severer than those by SGA users. It runs into the risk comparing an apple with an orange. Although the authors controlled many covariates, there can be many omitted (or unmeasured) covariates that are important in making conclusions.

4. Data reporting is acceptable.

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

Quality of written English: Needs some language corrections before being published

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.