Reviewer’s report

Title: A comparison of estimators from self-controlled case series, case-crossover design, and sequence symmetry analysis for pharmacoepidemiological studies

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Reviewer: Md. Jamal Uddin

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A comparison of estimators from self-controlled case series, case-crossover design, and sequence symmetry analysis for pharmacoepidemiological studies

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BMC Medical Research Methodology

In this manuscript, authors examine the impact of a time-varying confounder and its interactions with time-invariant confounders, time trends in exposures and events, and misspecification of risk period durations on the estimators from self-controlled case series (SCCS), case-crossover (CCO) design, and sequence symmetry analysis (SSA). The idea of the paper seems promising, however, I have several important major concerns:

1. Although in several articles (see below the ref) of the case only designs had already been mentioned such limitations (for example, SCCS design performs poor and provides bias in the case of the time-varying confounding) that the authors evaluated in this manuscript, my main concern here: what is NEW here? I would suggest reviewing more methodological papers of the SCCS, CCO and SSA and finding out key points that have not been addressed yet. For example: For SCCS, what will be happened if all subjects are censored at their first or last event or if the analysis is restricted to those subjects who experienced event after the start of exposure? Moreover, what will be happened if there is modest censoring at first or last event (up to 20%-40%)? In addition, how much bias shall we achieve if we remove different pre-exposure periods from the baseline?

2. Authors emphasis here the SSA methods method may be a suitable choice for applications in pharmacoepidemiological studies. However, it is difficult to say such general statement because a method can be performing very differently for different PE exposure, different databases and so on. Need a clear justification here.

Minor concerns:
3. Please add detail simulation codes in the appendix including possible explanations, so that reader can reproduce the results.

4. It is important to provide a clear compare and contrast between methods, at present it is missing.

5. Also, it would be easy for reader to understand, if authors provide a schematic representation of three methods (see blow an example: Uddin et al. International journal of clinical pharmacy 38.3 (2016): 714-723).

References:


Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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I am able to assess the statistics

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