Reviewer’s report

Title: The Effects of State Rules on Opioid Prescribing in Indiana

Version: 0  Date: 23 Oct 2016

Reviewer: Adrian Dunlop

Reviewer's report:

The submitted paper is a time series pre/post comparison of drug prescription data and census data in the state of Indiana.

While the authors have presented very important work - both from a clinical and policy perspective - especially given the increase in fatal opioid overdose across the USA and including in Indiana, the paper should not be accepted in its current form.

The authors use inappropriate language throughout - while changes pre and post the Implementation of the Drug Monitoring Program have been shown (though not clearly described), causation should not be inferred to this association - throughout the article the authors start with the assumption that a change has occurred, and state what the new policy has caused.

What they have observed, are different rates of prescribing, across different groups/doses/drugs, over time and claiming all these changes are from the change in policy/implementation of the monitoring program. They do not, in the introduction or discussion, adequately explain that no other events could impact on prescribing rates (they briefly mention in the discussion only) - this makes the article unpublishable in its current form.

Other suggestions to strengthen their findings:

* An analysis of data from another jurisdiction where a monitoring program was not implemented at the same time would strengthen the association. - neighbouring states are only briefly mentioned - without any supporting data provided or a reference provided

* Use of the (modified) Bradford Hill criteria to assess an association in a study that does not have an experimental design.

Terminology needs to be reconsidered throughout - for example

page 7, lines 4-9

" Thus, the difference in daily prescribing between the pre- and post-intervention period can be interpreted as a result of the rule change"
The fact that an interrupted time series analysis has been performed cannot, on its own, be used to infer causation.

Page 8 line 55
"the policy had a statistically significant negative impact on average MME per day per patient and the total MME dispensed in the state" - again causation should not be inferred

Page 9 lines 4-6
"This robustness check assures us that we are truly capturing the impact of the policy and not just an interruption in the time trend" - a statistical analysis technique cannot, on its own, remove all confounders and prove causation.

Regarding terminology
Suggest the term abuse is substituted for 'non-medical' use as abuse is no longer a DSM(5) term and can be open to misinterpretation. Also suggest the authors consider


Page 9 , lines 33-35
"This sensitivity analysis shows that our interrupted time series results are qualitatively robust" - the authors probably mean quantitatively - but again, this approach cannot remove all bias (known and unknown) - in fact throughout the authors use of the term qualitative is confusing - they do not present qualitative data

Table 1 is not explained in the text - while it is described as a regression, the columns header should describe what is in them. In fact all tables do not adequately describe what is being reported in each column.

Page 11, Lines 33-35
"a drug that experienced a significant negative post policy shock" - technically - a drug cannot receive a 'shock' - a drug is an object - the authors may be describing a pattern of prescribing behaviour

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

Yes

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

No

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

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

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