Reviewer’s report

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

Version: 1 Date: 18 Jan 2017

Reviewer: Chris Delcher

Reviewer's report:

Thank you for responding to my initial comments on the paper. I see that you have made important changes. However, I still have some concerns-

In the introduction (line 54), the authors indicate that little is known about provider perception or interpretation of the new rules which leads the reader to think that they have assessed perceptions in the paper, which they do not. I recommend removing this sentence. Same for the last sentence (line 63), I don't see how the paper evaluates how these "factors are associated with any interpretation of the emergency rules".

In line 67, please indicate that treatment of chronic pain is presumptive. No health diagnoses data are available to make this determination and is completely inferred from the prescribing data.

In line 70, please remove #3 as this study does not investigate underlying mechanisms. #2 can be expanded to include the various stratifications that are described.

Line 76, technically, the data are not de-identified as they contain dates of written Rxs. please describe as a "limited data set".

Line 90, thank you for the thorough discussion on Tramadol. However, I think it detracts from the paper and the sensitivity analysis at line 176 is sufficient.

Line 104, just describe as the "auto-regressive nature of the time series."

Line 112, I think the use of the term mediation analysis is confusing and should be removed. From what I can tell, the analysis did not test the effects on the coefficient of the primary outcome when these variables were entered into the model simultaneously but rather these were a series of new tests using different outcomes. A series of bivariate analyses was done. This should also be noted in the tables.

I don't think that Figure 2 is adding anything to the paper and given that it appears that three separate series are being tested, it is confusing. I suspect that the two lines shown below the dense part of the graph represent weekend prescribing. I think Figure 2 alone is sufficient.
I still do not feel comfortable with the way provider income is inferred in this analysis. Please note this in the limitations.

Line 202, please remove the header "underlying mechanisms".

Please use the phrase "emergency rules" consistently throughout.

In the discussion, please be careful about suggesting that the rules led to therapeutic intervention for patients. It could be that the regulatory burden of doing a full psychiatric workup, writing contracts, etc. led to providers deciding to turn patients away and not prescribe, rather than really evaluate the appropriateness of their prescribing. Figure 1 shows good evidence that prescribing behaviors changed and the authors should not over-interpret the data to suggest that this was beneficial across the board. For example, you may want to add that impacts on access-to-appropriate treatment and care involving opioid alternatives was not evaluated.

Table 2 still uses the term "narcotics", please adjust. Please indicate in the tables that these are unadjusted and/or bivariate analyses.

**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.

Yes

**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.

I am able to assess the statistics

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