Author’s response to reviews

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

Authors:
Morhaf Al Achkar (alachkar@iupui.edu)
Shaun Grannis (sgrannis@regenstrief.org)
Debra Revere (drevere@u.washington.edu)
Palmer MacKie (pmackie@iu.edu)
Meredith Howard (merhow@gmail.com)
Sumedha Gupta (sugupta@iupui.edu)

Version: 2 Date: 21 Oct 2017

Author’s response to reviews:

BHSR-D-16-00728R1

The Effects of State Rules on Opioid Prescribing in Indiana

Morhaf Al Achkar; Shaun Grannis; Debra Revere; Palmer MacKie; Meredith Howard; Sumedha Gupta

BMC Health Services Research

Dear Prof. Logan and Prof. Zalm,

Thank you for responding to our queries regarding our manuscript titled "The Effects of State Rules on Opioid Prescribing in Indiana" (BHSR-D-16-00728R1) that we had revised and resubmitted for review at BMC: Health Services Research in December 2016. We are very grateful for your decision to accept our manuscript for publication, conditional upon successful completion of revisions suggested by you and the reviewer. We are honored to have this opportunity and have carefully responded to each of the comments. Please find below our point-by-point response to the suggestions including details of how, and where in the manuscript we have made the requested changes and/or provided clarifications to address each of the suggestions.
We have also checked your website at http://bhsr.edmgr.com/, but have not found any additional comments that were saved as attachments.

We have submitted a revised manuscript, incorporating all the requested changes. We sincerely hope that our careful, detailed and timely revision, well in advance of the set deadline of 04 November 2017, will receive a favorable response. We feel privileged that this important work will be presented to all stakeholders through the platform of BMC: Health Services Research.

Sincerely,

Morhaf Al Achkar, Shaun Grannis, Debra Revere, Palmer MacKie, Meredith Howard and Sumedha Gupta.

I: Comments by Hilary Logan, PhD

Editor Comments:

1) Please note that the Consent to publish section is if you have shared identifying data about participants in your manuscript. As this is not the case for your manuscript, this section should read "Not applicable".

RESPONSE: This was changed to “Not applicable.”

2) Please ensure that the two SG authors are distinguishable in the Author contributions

RESPONSE: We have replaced the SG initials with the full names of the two authors to distinguish them in the Author contributions. Other author’s initials have been retained as such.

3) Please remove the figure legend from within the figure file, this should contain the image graphic only.

RESPONSE: We have removed the figure legend from figure file. It only contains the graph. The legend is provided at the end of the manuscript.
4) If the eTables are supplementary Tables, these should be uploaded as Additional files and not attached to the main manuscript.

RESPONSE: We reordered the tables to get rid of the distinction table and eTable.

BMC Health Services Research operates a policy of open peer review, which means that you will be able to see the names of the reviewers who provided the reports via the online peer review system. We encourage you to also view the reports there, via the action links on the left-hand side of the page, to see the names of the reviewers.

II: Reviewer reports: Chris Delcher (Reviewer 1):

1. 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".

RESPONSE 1: We have removed the statements about the `interpretation of the emergency rules’ from what were lines 54 and 63. Thank you for pointing this out.

2. 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.

RESPONSE 2: We have changed what was previously line 67 and is now line 61 to remove the mention of ‘chronic pain’. The statement is modified to say, “We sought to investigate the impact of Indiana's new emergency prescribing rules on prescription of opioids.” We agree with you that the modified statement reflects more accurately what we can capture with our data.

3. In line 70, please remove #3 as this study does not investigate underlying mechanisms.
RESPONSE 3: Done.

4. #2 can be expanded to include the various stratifications that are described.

RESPONSE 4: Per your suggestions we have expanded # 2 and added the dimensions along which stratified analyses is conducted – by patient gender, age, payer and zip code level aggregate measures of socioeconomic status.

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

RESPONSE 5: We have changed ‘de-identified data’ to the more correct ‘limited data set’ in what was line 76 and is now line 71.

6. 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.

RESPONSE 6: We have removed the detailed discussion on Tramadol from what was line 90 and is now line 86.

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

RESPONSE 7: We have changed “auto-regressive nature of prescribing behavior for patients and providers” to "auto-regressive nature of the time series." in what was previously line 104 and is now line 92.

8. 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.

RESPONSE 8: We have completely removed the term mediation analysis from manuscript, including eTable 3. What was line 112 has been modified to what is now line 99 and the term ‘mediate’ has also been removed from the Results section in the Abstract (new line 26). We have also changed mediation to correlation when we talk about the association between provider aggregate socioeconomic data and number of opioid prescriptions. This correction also partially addresses the concern raised in comment 10 below.

9. 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.

RESPONSE 9: We think you meant Figure 1 alone is sufficient. We have removed Figure 2 now. You noted correctly that the two lines below the dense part of the graph were capturing weekend prescriptions. Thank you for the suggestion. It makes the manuscript clearer and also more concise.

10. I still do not feel comfortable with the way provider income is inferred in this analysis. Please note this in the limitations.

RESPONSE 10: We understand your concern and share it. Per your suggestion we have made a note of this limitation in line 297 of the manuscript. We note, ‘Further, prescriber zip codes in our data could capture location of the prescriber’s residence or practice, which limits our ability to precisely interpret the positive association between zip code aggregate socioeconomic status and opioid prescribing changes.’

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

RESPONSE 11: Done.
12. Please use the phrase "emergency rules" consistently throughout.

RESPONSE 12: We have made changes in lines 12, 23, 30, 32, 53, 78, 88, 129, 130, 132, 139, 142, 161, 171, 195, 198, 199, 208, 209, 215, 218, 221, 226, 228, 253, 259, 279, 315 and in the captions of all the Tables and Figure 1. Now the phrase "emergency rules" has been used consistently throughout the manuscript.

13. 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.

RESPONSE 13: We agree with you. The emergency rules may have the unintended consequence of further creating barriers to access to adequate pain management. We have clarified this point in two ways in the Discussion section. First, in line 230 we have clarified that ‘reduction in inappropriate opioid dispensing lower rates of opioid misuse and non-medical use’. Second, we have elaborated on this further as a limitation of the study and noted in line 303 that ‘the added regulatory burden of opioid prescribing following the emergency rules may deter providers from prescribing altogether, resulting in worsening of patient pain outcomes.

14. 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.

RESPONSE 14: We have made the suggested addition in line 306 where we have clarified that ‘The impact of the emergency rules on access-to-appropriate treatment and care involving opioid alternatives could not be evaluated using our current data and is left to future work’. Thank you for the suggestion.

15. Table 2 still uses the term "narcotics", please adjust. Please indicate in the tables that these are unadjusted and/or bivariate analyses.
RESPONSE 15: Thank you for pointing out this error. We have changed narcotics to the more appropriate term ‘opioids’ in Table 2. We have also added details in the Table captions, notes or both clarifying if the estimates are from unadjusted and/or bivariate analysis.