Author's response to reviews

Title: Retrospective Analysis of the Diagnostic Yield of Newborn Drug Testing

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Version: 2
Date: 12 May 2014

Author's response to reviews: see over
May 12, 2014

Re: Manuscript 2145143133115304

Dear sir or madam,

We, the authors, of the above referenced manuscript have received your comments and critiques. We appreciate your time and thoughtful observations. Below please find our detailed responses to your concerns below. In the revised manuscript, we have highlighted areas of revised wording with yellow highlighting and additional of new content with double underlining. Tables 1-3 have been substantially revised.

**Reviewer 1:**

**MAJOR COMPULSORY REVISIONS:**

1. Abstract, Conclusions (…and throughout manuscript): Authors should always be careful about speaking in absolutes. For example, the statement "...will detect almost all prenatal non-medical drug exposures' needs to be 'softened'. It is rare that one study can universally answer a question and provide the definitive answer. This study is no different, especially considering the bivariate analyses that were performed (i.e., other variables were not controlled for using multivariable analyses). Therefore, please consider ‘softer’ language, such as "...may detect many cases” or other preferred language.

Language has been softened in Conclusions of Abstract and body of main manuscript.

2. Statistical analysis: The authors have done a nice job of presenting four comparison groups in their tables. However, these groups are not clearly defined for the reader in the methods section of the manuscript. Please correct.

Figure 1 has been revised to better indicate the groups, which are now labeled Group A, Group B, Group C, and Group D in Figure 1 and Tables 1 and 3. The methods explain these in detail. The Results section refers to these groups as well and references the appropriate figures and tables.

3. Statistical analysis: The authors clearly mention the inclusion of post hoc analyses, yet never explain any details to the reader. Please correct.

In response to critiques from reviewer #2, maternal age and gestational age have been converted to median and range rather than mean +/- standard deviation. Consequently, ANOVA analysis no longer applies.

**MINOR ESSENTIAL REVISIONS:**

4. Discussion: The authors mention a lack of clear evidence for cannabinoids causing adverse effects during pregnancy. However, the American Psychiatric Association
Guidelines state an “increasingly robust evidence that marijuana use during pregnancy is associated with a number of deleterious outcomes (APA, 2006). Please ensure a balanced discussion is provided.

This has been corrected to include the long term adverse effects of cannabinoids on learning, attention and behavior.

5. Table 2: The term “Breakdown” seems colloquial. Please choose more professional language for the table title.

This has been changed to “Categorization”.

6. References: There are a number of careless mistakes (e.g., incomplete references, such as #5 and #20). Please correct.

References have been corrected.

DISCRETIONARY REVISIONS:
7. All manuscript sections: The authors use a fair amount of discipline-specific jargon (e.g., gravida, para) that may not be familiar to all readers (i.e., outside of the core audience for this particular journal). Recommend clarifying jargon for the reader, when feasible.

Gravida and para have been defined in Methods and in the legend of Table 1.

8. Figure 2A: This particular chart is easy to read over the computer display, but when printed in black-and-white, it is much more difficult to read (i.e., without patterns within the bars, or other distinguishing features).

This figure has been revised for better display (reviewer #2 also had similar critique of this figure).

Reviewer 2

Major Compulsory Revisions:

1. Methods: clarify if the use of the assessment tool was used throughout entire study period: “… is based on assessment of 29 items related to … and newborn risk factors, which was implemented on [date] (see Additional File 1).”

The same tool was used throughout the entire period of study. We have added the following to the first paragraph of Methods:
“The assessment tool was implemented in 2007 (prior to period of retrospective study in this report) and used throughout the entire period of retrospective analysis.”

2. Results – under Yield of Screening Criteria: this section needs a substantial addition of content. Discussion draws conclusions on the risk factors that are never presented in this section.
We have substantially expanded this section, incorporating the statistical analyses summarized in Table 3.

3. Discussion: Last sentence of second paragraph: No mention of specificity of testing anywhere else prior to this. You need to substantiate this. What was the specificity of the test prior to inclusion of those factors? What was it after?

This sentence was removed as the paper does not address the specificity of the risk assessment tool.

4. Discussion: 7th paragraph: you need to add to this a discussion on how urine drug screening also failed to detect non-medical drug use found in meconium testing.

We have added the following to this paragraph:
“In addition, urine drug testing failed to detect 128 cases of non-medical drug use determined by meconium analysis.”

5. Discussion: 8th paragraph: elaborate on the limitation of: “only newborns meeting protocol criteria had screening ordered”

We had added the following clarification to this sentence:
“Only newborns meeting protocol criteria had screening ordered (i.e., 63.2% of the live birth in the University of Iowa sample did not have newborn drug testing done as they did not meet any of the risk criteria).”

6. Discussion: Add to the discussion a part regarding unexpected findings shown in Table 3 such as the “Total including poor prenatal care and social risk factors” being relatively high for the “No drug(s) or metabolite(s) detected”

This is now added to the Discussion.

Minor Essential Revisions:

1. Background: Change percentage in opening sentence to a rate.

This has been changed as suggested.

2. Background: Last sentence, second paragraph: change “states” to either “hospitals”, “providers”, or “practitioners”.

This has been changed to “providers”.

3. Background: Remove the single quotes from “‘gold standard’”.

This has been changed.
4. Background: Stay consistent with use of “ethanol” or “alcohol”

We changed to “ethanol” throughout.

5. Background: 5th paragraph, 1st sentence needs revised. Consider: Protocols for identifying which newborns to screen present a number of challenges for the clinical and social work team.

We have made the suggested change.


This change has been made.

7. Methods: Include sample size in first sentence: “(n=___)”

This is now included.

8. Methods: Elaborate on random selection process to select the 200 charts where no drug was detected

This is now described in Methods.

9. Methods: 2nd paragraph, 2nd sentence: include sample size of patients with urine but no meconium testing

This is now included.

10. Methods, Under drug testing analysis: Get rid of “(e.g. no false positives)” in 1st paragraph, last sentence. Suggestion: “…methods agreed eliminating likelihood of false positives.”

We have made the suggested change.

11. Results: Insert “(n=___)” where you have % only.

We have made the suggested insertion.

12. Results: 1st paragraph, 1st sentence: remove unnecessary comma after “both”

We have made the suggested change.

13. Results: 1st paragraph, 2nd sentence: after “…87.6% and 74.6%, respectively” add statement about resulting sample size.

We have made the suggested insertions.
14. Results: 3rd paragraph, 1st sentence: remove the “or” and place “23.3%” in parentheses

We have made the suggested change.

15. Results: 3rd paragraph: add a statement that all positives were confirmed positive by GC/MS or LC/MS/MS to be consistent with the finding in urine section

This change has been made.

16. Results: Under Findings in urine, 3rd sentence needs rephrase to something like: “Nine of those samples were confirmed positive by …. and the other 3 urine specimens screened positive for THC…” As is, the “All confirmed positive” beginning is misleading.

This section has been edited as suggested.

17. Results: Under Findings in Urine: for sentence starting with “In 128 cases” add clarification whether meconium analysis was confirmed positive or not. As it reads, it is unclear whether urine or meconium results are true.

All were confirmed positive in meconium. This clarification has been made.

18. Results: Under Findings in Urine, 2nd paragraph: reword 1st sentence. Suggestion: An additional 354 newborns had urine drug testing performed in the absence of meconium testing.

The suggested edit has been made.

19. Results: Under Yield of Screening Criteria: replace “categorical criteria” to something more descriptive. Suggestion: various risk factors from the assessment tool

The suggested edit has been made.

20. Results: Under Yield of Screening Criteria: replace % at end of 2nd sentence to reflect the % of “all but 7” not the % of “7.” Add the “3.1% to the next sentence after “7”

The suggested edit has been made.

21. Discussion: Last paragraph, 3rd sentence: “(e.g....)” not appropriate. Reword to something like: “Specimens can be held for up to 2 weeks allowing…”

The suggested edit has been made.

22. Figure 1: add % whenever n is given

This has been done. The figure legend provides details on how percent is calculated.
23. **Table 2:** the superscript “1” in the title describes that all non-medical drug use was a result of unintended (non-medical) use of prescription drugs. Either remove the place somewhere more appropriate or reword the explanation to state that when drug used was a Rx, it was confirmed that the Rx was used for non-medical reasons as “clearly established….”

Superscript has been moved. The additional description to the table encompasses the edits suggested.

24. **Figure 2:** hard to distinguish color in key because color scheme does not vary enough. Either choose different variety of gray scale or print in color

This figure has been revised for better display (reviewer #1 had similar critique).

25. **Figure 2:** Add a title to entire Figure 2 (in addition to titles for A and B)

Overall title has been added to this figure.

26. **Figure 3:** Hard to distinguish color in key because color scheme does not vary enough. Either choose different variety of gray scale or print in color

Figure 3 has been converted to black and white with better differentiation between groups.

27. **Figure 3:** Add some statistical comparison

Statistical comparison has been added to Figure 3; this parallels data in Table 3. This figure has also been revised to delineate the Groups A, B, C, and D referenced in the manuscript text and Tables 1 and 3.

28. **Figure 3:** Add a title

Title has been added.

29. **Table 3:** Change superscripts so they are listed in numerical order as you read down the table

This change has been made.

30. **Table 3:** Explain bolded numbers

Numbers are no longer in bold as was not necessary.

If more elaboration or detail is needed, please contact me and I am happy to help.

Sincerely,