

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Maternal trauma due to motor vehicle crashes and pregnancy outcomes: A systematic review and meta-analysis
AUTHORS	Amezcu-Prieto, Carmen; Ross, Jennifer; Rogozińska, Ewelina; Mighiu, Patritia; Martínez-Ruiz, Virginia; Brohi, Karim; Bueno Cavanillas, Aurora; Khan, Khalid; Thangaratinam, Shakila

VERSION 1 – REVIEW

REVIEWER	Richard Brown McGill University, Canada
REVIEW RETURNED	22-Nov-2019

GENERAL COMMENTS	<p>This is a thorough and comprehensive meta-analysis of the studies describing the maternal and fetal consequences of maternal involvement in a motor vehicle accident. The aims are clearly stated as are the conclusions and the limitations.</p> <p>The one major concern I would raise relates to the population being evaluated. It should perhaps be more strongly emphasized that these data apply to developed countries in the main - only one of the papers included data from an under-developed country. It could perhaps be argued that this study should have been excluded or evaluated independently, as many factors in the the underdeveloped world will more profoundly influence outcomes [motor vehicle and road safety standards and access to healthcare primarily] over and above the events themselves. Including just one study from such populations does not allow the outcomes in the underdeveloped world to be adequately represented whilst influencing perhaps the outcomes that might otherwise be seen in the developed world.</p> <p>There are a few minor typographical or grammatical issues that might be corrected before final acceptance for example only on Page 4 Line 28 "in a[n] collision" Line 46 "more data [is] are required" etc.</p>
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REVIEWER	Reem Malouf Oxford University
REVIEW RETURNED	06-Jan-2020

GENERAL COMMENTS	<p>This is a very good review concerning important and interesting question.</p> <p>Please could the authors provide a justification/explanation for the significant level of heterogeneity which exists across most of the pooled outcomes.</p> <p>Other minor suggestions:</p> <ol style="list-style-type: none">1) Add a new subheading after the background to clarify the review objectives.
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	2) For method - could add the review inclusion criteria.
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REVIEWER	Julie Morris University of Manchester
REVIEW RETURNED	29-Feb-2020

GENERAL COMMENTS	<p>This systematic review and meta-analysis looks at the relationship between involvement in a motor vehicle crash and maternal/fetal outcomes.</p> <p>There are a number of issues relating to the methodology and reporting of the results which need to be resolved.</p> <ol style="list-style-type: none"> 1. It is not clear whether single or double screening of papers was carried out. This should be confirmed. Screening by two independent researchers is the gold-standard recommended procedure. 2. More information should be presented on the 19 studies included in the systematic review. For example, in the case of the 'incidence' studies (n=12), it would be useful to give the individual study incidences for the outcomes shown in Table 2. For the 'comparative' studies the individual numbers of events and case/control numbers should be included in the forest plots (see Figure 3). 3. The current reporting of the meta-analysis results relating to fetal deaths needs to be amended. It is not appropriate to state that, "...pregnant women involved in MVC using seatbelts have a lower risk of fetal death" (Abstract and Results). The 95% confidence interval for the associated OR includes 1, and hence the relationship between MVC and fetal death is not statistically significant. In addition, it is not appropriate to state that pregnant women involved in MVC have a higher risk of fetal death (Abstract), as again the associated OR includes 1. 4. The conclusions of the meta-analysis should be modified with the caveat that the results are based on a very small number of studies (often just two studies), with one of the main results (association with maternal death) based on one study.
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VERSION 1 – AUTHOR RESPONSE

Reviewer:

Reviewer Name: Richard Brown

Institution and Country: McGill University, Canada

This is a thorough and comprehensive meta-analysis of the studies describing the maternal and fetal consequences of maternal involvement in a motor vehicle accident. The aims are clearly stated as are the conclusions and the limitations.

- The one major concern I would raise relates to the population being evaluated. It should perhaps be more strongly emphasized that these data apply to developed countries in the main - only one of the papers included data from an under-developed country. It could perhaps be argued that this study should have been excluded or evaluated independently, as many factors in the underdeveloped world will more profoundly influence outcomes [motor vehicle and road safety standards and access to

healthcare primarily] over and above the events themselves. Including just one study from such populations does not allow the outcomes in the underdeveloped world to be adequately represented whilst influencing perhaps the outcomes that might otherwise be seen in the developed world.

Answer: Thank you for your suggestion. We have considered this issue in the limitations of the study, in Page 11, line 292 to 294: 'As a fifth point, these data apply to developed countries - only one of the papers included data from an underdeveloped country, perhaps influencing the outcomes that might otherwise be seen in the developed world'.

- There are a few minor typographical or grammatical issues that might be corrected before final acceptance for example only on Page 4 Line 28 "in a[n] collision. Line 46 "more data [is] are required" etc.

Answer: Thank you, It is corrected in Page 4, line 90 and 100.

Reviewer: 2

Reviewer Name: Reem Malouf

Institution and Country: Oxford University

This is a very good review concerning important and interesting question.

- Please could the authors provide a justification/explanation for the significant level of heterogeneity which exists across most of the pooled outcomes.

Answer: Thank you for highlighting this matter. It is not uncommon for a meta-analysis of observational designs to encounter a high level of statistical heterogeneity with a wide range of reasons for its occurrence (Colditz et al. 1995. Am J Epidemiol 142(4): 371-382). In anticipation of this issue, we applied a random-effects model that takes into account between-study variation and quantified the degree of the variation. (see Methods) Nevertheless, we recognise that there is insufficient discussion of the reported levels of heterogeneity. We have now addressed that by incorporating following sentences in the discussion: "Despite analysing the data within the respective study designs and incorporation of anticipated variation into the statistical model (random-effects)(46), we encountered substantial statistical heterogeneity in the pooled estimates that could not be formally explored due to a limited number of studies and poor reporting of important factors such as trauma severity." (Page 11, Lines 288-292); and in the conclusion section: "However, these findings need to be treated with caution due to considerable between-study differences." (Page 13, Lines 337-338). Additionally, in Fig. 3 we added the information on the type of the model (random-effects) to emphasise that the between-study heterogeneity was anticipated and taken into account in the meta-analysis.

Other minor suggestions:

1) Add a new subheading after the background to clarify the review objectives.

Answer: We have included this subheading in Page 5, Line 111.

2) For method - could add the review inclusion criteria.

Answer: It is included in Page 6, Line 138 to 143: 'Papers were selected if they studied the effects of exposure to trauma due to involvement in an MVC during pregnancy vs. non-exposure, with follow up to verify outcomes in various settings including secondary care, collision and emergency, and inpatient care. Observational studies (cohort studies, case-control design, non-intervention arms of randomised controlled trials) were included. Case series and case reports were excluded. Appendix 1 shows the search strategy for Medline (via Ovid) and Appendix 2 the excluded studies with reasons'.

Reviewer: 3

Reviewer Name: Julie Morris

Institution and Country: University of Manchester

This systematic review and meta-analysis looks at the relationship between involvement in a motor vehicle crash and maternal/fetal outcomes. There are a number of issues relating to the methodology and reporting of the results which need to be resolved.

1. It is not clear whether single or double screening of papers was carried out. This should be confirmed. Screening by two independent researchers is the gold-standard recommended procedure. Answer: It was a double screening of papers. We have included in the manuscript. Page 6, Line 146.

2. More information should be presented on the 19 studies included in the systematic review. For example, in the case of the 'incidence' studies (n=12), it would be useful to give the individual study incidences for the outcomes shown in Table 2. For the 'comparative' studies the individual numbers of events and case/control numbers should be included in the forest plots (see Figure 3).

Answer: It is amended in Table 2 and Figure 3, according to your suggestions.

3. The current reporting of the meta-analysis results relating to fetal deaths needs to be amended. It is not appropriate to state that, "...pregnant women involved in MVC using seatbelts have a lower risk of fetal death" (Abstract and Results). The 95% confidence interval for the associated OR includes 1, and hence the relationship between MVC and fetal death is not statistically significant. In addition, it is not appropriate to state that pregnant women involved in MVC have a higher risk of fetal death (Abstract), as again the associated OR includes 1.

Answer: Thank you for your comment. It is now amended in Abstract and Results.

4. The conclusions of the meta-analysis should be modified with the caveat that the results are based on a very small number of studies (often just two studies), with one of the main results (association with maternal death) based on one study.

Answer: Thank you for your observation. We conclude as follows in the manuscript: Pregnant women involved in MVC seem to be at increased risk of maternal death and complications, especially placental abruption, than those not involved in MVC. The risk of complications such as preterm delivery, premature rupture of membranes and caesarean section were also increased. However, these findings need to be treated with caution due to considerable between study differences. Road traffic authorities should be conscious and strict in targeting preventive measures aimed at pregnant users of motor vehicles due to risk associated with potential involvement in MVC'.

VERSION 2 – REVIEW

REVIEWER	Richard Brown McGill University, Montreal
REVIEW RETURNED	09-Apr-2020
GENERAL COMMENTS	I believe the authors have adequately addressed all the prior issues raised in the initial review
REVIEWER	Julie Morris University of Manchester, UK
REVIEW RETURNED	10-Apr-2020
GENERAL COMMENTS	This paper has been revised to take account of the majority of the statistical issues raised in my original review. I would just suggest a slight amendment to the Conclusions: Replace,

	"However, these findings need to be treated with caution due to considerable between study differences", with "However, these findings need to be treated with caution due to the small number of studies included in the review and considerable between study differences"
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Richard Brown

Institution and Country: McGill University, Montreal

I believe the authors have adequately addressed all the prior issues raised in the initial review

Answer: Thank you.

Reviewer: 3

Reviewer Name: Julie Morris

Institution and Country: University of Manchester, UK

This paper has been revised to take account of the majority of the statistical issues raised in my original review.

I would just suggest a slight amendment to the Conclusions:

Replace,

"However, these findings need to be treated with caution due to considerable between study differences",

with

"However, these findings need to be treated with caution due to the small number of studies included in the review and considerable between study differences"

Answer: Thank you. Changes can be found in the conclusions, page 13, lines 323 and 324.