

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Socio-demographic characteristics of women sustaining injuries during pregnancy, A Study from the Danish National Birth Cohort
AUTHORS	Jasveer Virk, Paul Hsu and Jorn Olsen

VERSION 1 - REVIEW

REVIEWER	Peter E. Fischer, M.D., M.S. Fellow, Surgical Critical Care Oregon Health and Science University Portland, OR
REVIEW RETURNED	30/01/2012

GENERAL COMMENTS	<p>Virk and colleagues present an excellently written cohort study examining injury and adverse birth outcomes in women enrolled in the Danish National Birth Cohort. The study population consists of women who were contacted to enroll by the primary physician caring for them during their pregnancy. In the cohort of over 80,000 women, 3.2% of women were injured at least once during their pregnancy. The only statistically significant finding was that women with severe head injuries were more likely to have fetal demise than their uninjured counterparts. Other adverse birth outcomes were not increased in the injured population. I do have several comments / questions for the authors.</p> <ol style="list-style-type: none">1. Patients with pre-eclampsia and diabetes were excluded from the study population. This was a fairly large group making up over 10% of the National Birth Cohort. Was there any consideration to adjust for these conditions in the model rather than exclude them from analysis? Was the rate of injury in these excluded women similar to the studied population?2. The severity of injury was based on admittance to the emergency department vs. other hospital department. Were those who were seen originally in the emergency department subsequently discharged and these were considered the less injured? What are the admitting practices of physicians in Denmark? Are pregnant women more likely to be admitted for minor injury? Is there any change in admitting practices based on gestational age?3. One of the largest risk factors for a pre-term birth is previous per-term birth. Was any of the previous birth history of the mother available and was this adjusted for in the model?4. The rate of injury (3.2%) was approximately half that of previous studies including a recently published similar population-based study (Fischer). Do you have any reasons for that? Do you think that since to be in the study the women by default had a primary care physician that patients with minor injury would report to their PCP rather than the ED and not be captured in the National Patient
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	<p>Registry?</p> <p>5. Please address the applicability of this study to other populations. This cohort was affluent and not similar to the general trauma population especially seen in the United States. Over half were high or middle grade professionals and 99% had partner cohabitants. In the U.S., these women were significantly less likely to be injured (Fischer).</p> <p>6. In Table 1, the "Other Place of Injury" group has an n of 78,297. Shouldn't this n be total injured patients (2,604) minus those seen only in the ED (2,577)? If these women are uninjured why are they being treated?</p> <p>7. Please reference Table 3 in the manuscript.</p> <p>This study is an important contribution to the literature concerning injury in pregnant women. Far too often these studies are based solely on trauma registry data and fail to capture those evaluated only in the emergency department. Further population-based large cohort studies need to be conducted to determine the true effect of minor and severe injury in the pregnant woman.</p> <p>Reference: Fischer PE, Zarzaur BL, Fabian TC, Magnotti LJ, Croce MA. Minor Trauma is an Unrecognized Contributor to Poor Fetal Outcomes: A Population-Based Study of 78,552 Pregnancies. J Trauma. 2011;71(1):90-93.</p>
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REVIEWER	<p>Erin K. Sauber-Schatz, PhD, MPH LCDR, US Public Health Service Senior Research Scientist Motor Vehicle Injury Prevention Team Division of Unintentional Injury Prevention National Center for Injury Prevention and Control, CDC, USA</p>
REVIEW RETURNED	28/02/2012

THE STUDY	<p>Methods adequately described: There is no mention of why the adjustment variables were picked and whether or not they were significant to the model. Additionally no comment was made on how clustering was or was not handled for women who had more than one birth during the study period. Was the study period 1996-2002? It is mentioned that the cohort was established during those years, but it is not stated what years of data were used. Also important factors such as previous preterm birth (on three levels yes, no, no prior birth) and previous low birth weight were not included in the model. These are well established risk factors and should have been included or discussed. Also the cut offs used for outcomes are not standard cut offs. Normal birthweight is usually ≥ 2500 grams not >2500 grams. The preterm cutoffs are too broad. I would suggest at least looking at <34 weeks (if not breaking this one up further), 34-36 weeks, and ≥ 37 weeks. No discussion of why Apgar cutoffs were chosen at <10. Some literature exists discussing outcomes of infants at various Apgar scores. The authors should consider a different cut off such as 7-explore the literature and give support to your cut off decisions.</p> <p>Key Message-First one "Pregnant women were slightly..." Pregnant women or Pregnant women who were injured? You are missing the exposure and main point of the study by not stating this.</p>
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	<p>Strengths and limitations-first point. The women are taken from a general population, but you are still selecting women from the health care system. You are not capturing all injuries in the population only those who sought care; therefore, I don't think your statement is accurate as stated.</p> <p>Methods appropriate: Discussion of reasons behind different analyses (HR vs. OR) is not provided, clustering is not discussed, adjustment variables missing key risk factors.</p>
RESULTS & CONCLUSIONS	<p>I wanted to respond maybe to several of these questions. I don't think the cutoffs used in several instances are the best cutoffs for the outcomes of interest. In addition, the limitations of the methods that I previously discussed makes me question the credibility of the results. The presentation of the results needs some work. The tables should be stand alone, but the adjustment variables (or that the HR and OR were adjusted at all) are not indicated in the table 3 and reference groups for the women with head and neck injuries and women with head injuries are unclear.</p> <p>The paper results and conclusions are not clear because there is not enough discussion to why this paper's findings vary from references 8-23. That is a lot of literature that counters your findings and the authors don't spend enough time discussing why they think their findings differ. Also in light of the categorization of the outcome variables I don't think the results are clear.</p>
GENERAL COMMENTS	<p>Below are general comments and suggested edits. Some are in repetition of what was discussed above</p> <ol style="list-style-type: none"> 1. Key Messages first bullet-indicate you are talking about injured pregnant women 2. Strengths and Limitations-first bullet you use a general population, but you are pulling you injuries from the health care system. Consider rephrasing/tightening this statement. 3. Abstract: Results "Injured pregnant women..." results are written in terms of the pregnant women and not their infants consider adding "...likely to deliver infants that were stillbirth..." 4. Abstract: Conclusion-nothing in the methods describes why it is only injuries "among moderately affluent women" explain or keep this detail out of the abstract. 5. Introduction-is sparse with not mention of how different mechanisms of injuries can cause different outcomes. May want to considering pulling some of the background information from the discussion section to the introduction and then just re-reference in the discussion. 6. Methods-what years of data were used for this study? 7. Methods-How many women had more than one birth during the study time period? How was this handled in the analyses? 8. Methods-preterm birth cutoffs should be reconsidered. Term birth is ≥ 37 weeks, late preterm is considered 34-36 weeks, early preterm can be < 34 weeks and you can break this up further to look at the associations. Look at prior studies in the area and especially in current Maternal and Child Health literature to be sure you are using the most current cutoffs suggested (and cite it). 9. Methods-low birth weight again the cut-offs are not in line with maternal and child health literature ≥ 2500 grams is normal birth weight, low birth weight is 1500-2499 and very low birth weight is < 1500 grams. 10. Methods-what is the source of your adjustment variables? Birth records? What is your rationale for including these variables? What is their significance to the model?

11. Methods-previous preterm birth and previous low birth weight are important factors that should have been considered in the model.
12. Methods-Apgar score. I think the cut off value should be reconsidered. See the literature for Apgar cutoffs and NICU admission-this may help guide you for a more appropriate cut off. By including any infant <10 you are diluting possible findings. Look at the distribution of infants by Apgar score in your data. I would say a majority of them will be in the 7-10 range.
13. Methods-what are "other departments" also see the literature, there is a bias for pregnant women to seek care. I would also suggest you look at your distribution of women by trimester and see where women received their treatment. Are more women who are in their 3rd trimester going to the ED vs. other places? There may be a bias here by trimester.
14. Results "injured women were younger..." were these statistically significant differences? Please state significance and give p-values.
15. Results "Approximately one third..." give actual percents in this statement and the next.
16. Results "We found that injured..." again state this in terms of the infants.
17. Results "To assess severity..." this is really a methods statement. Just give us the results such as "When assessing for severity of injury..."
18. Results "Place of treatment was not adversely related to SGA.." what do you meant by not adversely related to SGA.
19. Consider stratifying by trimester, do results differ?
20. Discussion-why unselected population-women are still self selecting by seeking treatment
21. Discussion-why affluent? Never discussed as to why they are affluent-I thought whole population was included
22. Discussion-References 8-23 found adverse pregnancy outcomes resulting from maternal injury. Why do you think your study differs? Not enough discussion of why your findings might differ from the literature.
23. Discussion-paragraph beginning "Unlike many previous..." Discuss the implications of what your data showed. What reasons do you think you found these differences?
24. Discussion what is the reference for "None out of ten traumatic injuries during pregnancy are minor"? Is it 16 also?
25. Discussion-"While previous studies on pregnant injured women..." This sentence doesn't make sense to me. You are stating that other studies have focused out several stated outcome and then you say this study addresses socio-demographic characteristics-this isn't an outcome. Are you trying to say that you considered socio-demographic characteristics in your assessment of outcomes? Please clarify.
26. Discussion- Future studies...may influence susceptibility to injury severity and injury proneness" why? For prevention purposes?
27. Table 1. indicate what place of treatment other includes
28. Table 1. Lots of data that isn't used/adjusted for in the paper-fine to show just commenting that some of this may contribute to the model. Numbers for previous adverse pregnancy outcomes would be a nice addition
29. Table 2-what is a vital activity?
30. Table 3-This table needs to be able to stand on its own.
31. Table 3. Neither the title or table notes that the ORs and HRs are adjusted and for what factors they are adjusted for.
32. Table 3 I would suggest changing abnormal to adverse in the title.

	<p>33. Table 3 There needs to be labeling for which values are ORs and which are HRs and indication that there are 95% CIs.</p> <p>34. Table 3 References for the head/neck injuries and head injury calculations is not clear.</p> <p>This is an important study that would be a worthwhile publication after addressing reviewer's comments/concerns.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer #1: Peter E. Fischer

1. Patients with pre-eclampsia and diabetes were excluded from the study population. This was a fairly large group making up over 10% of the National Birth Cohort. Was there any consideration to adjust for these conditions in the model rather than exclude them from analysis? Was the rate of injury in these excluded women similar to the studied population?

These women have been added back into the analyses, and these conditions are adjusted for in the analyses.

2. The severity of injury was based on admittance to the emergency department vs. other hospital department. Were those who were seen originally in the emergency department subsequently discharged and these were considered the less injured? What are the admitting practices of physicians in Denmark? Are pregnant women more likely to be admitted for minor injury? Is there any change in admitting practices based on gestational age?

If injuries are severe, pregnant women would be transferred from the emergency department and admitted. We do not know if women are more likely to be admitted for minor injury, or if admittance practice differs based on gestational age. It is likely that the biggest factor influencing injury, is severity of injury and potential harm to the fetus.

3. One of the largest risk factors for a pre-term birth is previous per-term birth. Was any of the previous birth history of the mother available and was this adjusted for in the model?

This data is available, and we have adjusted the model for preterm birth to include history of preterm births.

4. The rate of injury (3.2%) was approximately half that of previous studies including a recently published similar population-based study (Fischer). Do you have any reasons for that? Do you think that since to be in the study the women by default had a primary care physician that patients with minor injury would report to their PCP rather than the ED and not be captured in the National Patient Registry?

Yes, minor injuries seen in family practice would not be registered into the National Patient Registry.

5. Please address the applicability of this study to other populations. This cohort was affluent and not similar to the general trauma population especially seen in the United States. Over half were high or middle grade professionals and 99% had partner cohabitants. In the U.S., these women were significantly less likely to be injured (Fischer).

We have added a statement that addresses applicability to other populations.

6. In Table 1, the "Other Place of Injury" group has an n of 78,297. Shouldn't this n be total injured patients (2,604) minus those seen only in the ED (2,577)? If these women are uninjured why are they being treated?

For this next version of the paper, we stratify table 1 and 3 on pregnant women who are injured, and pregnant women with head or neck injuries.

7. Please reference Table 3 in the manuscript.

Table 3 is now referenced in the manuscript.

8. Citation: Fischer PE, Zarzaur BL, Fabian TC, Magnotti LJ, Croce MA. Minor Trauma is an Unrecognized Contributor to Poor Fetal Outcomes: A Population-Based Study of 78,552 Pregnancies. J Trauma. 2011;71(1):90-93.

This citation has been added.

Reviewer #2: Erin Sauber-Schatz

1. Methods appropriate: Discussion of reasons behind different analyses (HR vs. OR) is not provided, clustering is not discussed, adjustment variables missing key risk factors.

We have clarified reasons for using hazard and odds ratios for this analysis.

2. I wanted to respond maybe to several of these questions. I don't think the cutoffs used in several instances are the best cutoffs for the outcomes of interest. In addition, the limitations of the methods that I previously discussed makes me question the credibility of the results. The presentation of the results needs some work. The tables should be stand alone, but the adjustment variables (or that the HR and OR were adjusted at all) are not indicated in the table 3 and reference groups for the women with head and neck injuries and women with head injuries are unclear.

Categories of preterm birth and low birth weight have been changed and reflect the reviewers' suggestions. Tables have been clarified to reflect adjustment variables and comparison groups are more clearly stated.

3. The paper results and conclusions are not clear because there is not enough discussion to why this paper's findings vary from references 8-23. That is a lot of literature that counters your findings and the authors don't spend enough time discussing why they think their findings differ. Also in light of the categorization of the outcome variables I don't think the results are clear.

Outcome variables have been re-categorized, and discussion has been lengthened.

4. Key Messages first bullet-indicate you are talking about injured pregnant women
The bullet has been changed.

5. Strengths and Limitations-first bullet you use a general population, but you are pulling you injuries from the health care system. Consider rephrasing/tightening this statement.
Denmark has universal health care coverage, so these women reflect the general Danish population.

6. Abstract: Results "Injured pregnant women..." results are written in terms of the pregnant women and not their infants consider adding "...likely to deliver infants that were stillbirth..."
This has been added.

7. Abstract: Conclusion-nothing in the methods describes why it is only injuries "among moderately affluent women" explain or keep this detail out of the abstract.
This detail has been taken out of the abstract.

8. Introduction-is sparse with not mention of how different mechanisms of injuries can cause different outcomes. May want to considering pulling some of the background information from the discussion section to the introduction and then just re-reference in the discussion.
We have added to our introduction a discussion of how different injuries/mechanisms cause adverse maternal/fetal outcomes.

9. Methods-what years of data were used for this study?
We define the study years in the first sentence of the methods section (1996-2002). Injuries during pregnancy and birth outcomes were all assessed during this time.

10. Methods-How many women had more than one birth during the study time period? How was this handled in the analyses?
Very few women, and for those women, we have entered *repeated subject* term to the model statements.

11. Methods-preterm birth cutoffs should be reconsidered. Term birth is ≥ 37 weeks, late preterm is

considered 34-36 weeks, early preterm can be <34 weeks and you can break this up further to look at the associations. Look at prior studies in the area and especially in current Maternal and Child Health literature to be sure you are using the most current cutoffs suggested (and cite it).

Categories of preterm birth have been changed and reflect the reviewers' suggestions.

12. Methods-low birth weight again the cut-offs are not in line with maternal and child health literature ≥ 2500 grams is normal birth weight, low birth weight is 1500-2499 and very low birth weight is <1500 grams.

These are the cutoffs we used in our analysis; we have changed '2499' to '2500' in the manuscript.

13. Methods-what is the source of your adjustment variables? Birth records? What is your rationale for including these variables? What is their significance to the model?

The various data sources (registers, and Danish National Birth Cohort) are clearly identified in the methods section.

14. Methods-previous preterm birth and previous low birth weight are important factors that should have been considered in the model.

History of preterm birth has been added to the pre-term birth model. History of low birth weight has been added to the low birth-weight model.

15. Methods-Apgar score. I think the cut off value should be reconsidered. See the literature for Apgar cutoffs and NICU admission-this may help guide you for a more appropriate cut off. By including any infant <10 you are diluting possible findings. Look at the distribution of infants by Apgar score in your data. I would say a majority of them will be in the 7-10 range.

We have changed our categorization of APGAR Score (<3, 4-6, 7-10).

16. Methods-what are "other departments" also see the literature, there is a bias for pregnant women to seek care. I would also suggest you look at your distribution of women by trimester and see where women received their treatment. Are more women who are in their 3rd trimester going to the ED vs. other places? There may be a bias here by trimester.

We did not have enough women that were injured to look at injuries by trimester.

17. Results "injured women were younger..." were these statistically significant differences? Please state significance and give p-values. Results "Approximately one third..." give actual percents in this statement and the next.

We have added a footnote to table 1 of the variables with p-values <0.05 comparing demographic variables in the injured and uninjured groups calculated by chi-square tests.

18. Results "We found that injured..." again state this in terms of the infants.

This statement has been reworded.

19. Results "To assess severity..." this is really a methods statement. Just give us the results such as "When assessing for severity of injury..."

This statement has been reworded.

20. Results "Place of treatment was not adversely related to SGA.." what do you mean by not adversely related to SGA.

This version of the paper is not looking at place of treatment; per reviewers comments we now focus our paper on all injuries and further stratify by head or neck injuries.

21. Consider stratifying by trimester, do results differ?

Unfortunately, the numbers in our study do not permit for a meaningful analysis when stratifying

injuries by trimester as the number of exposed cases is too small.

22. Discussion-why unselected population-women are still self selecting by seeking treatment
We have clarified our intent behind using the term 'unselected population'.

23. Discussion-why affluent? Never discussed as to why they are affluent-I thought whole population was included.

The entire population of Denmark has not been used; the Danish National Birth Cohort is based on approximately 100,000 women. In general, the Nordic countries are affluent; they have generous social welfare programs, low fertility, and a universal health care coverage that is available at no cost to patients.

24. Discussion-References 8-23 found adverse pregnancy outcomes resulting from maternal injury. Why do you think your study differs? Not enough discussion of why your findings might differ from the literature.

We have added to the discussion section the differences between the Danish population when comparing to other populations.

25. Discussion-paragraph beginning "Unlike many previous..." Discuss the implications of what your data showed. What reasons do you think you found these differences?

This sentence has been reworded.

26. Discussion what is the reference for "None out of ten traumatic injuries during pregnancy are minor"? Is it 16 also?

Yes.

27. Discussion-"While previous studies on pregnant injured women..." This sentence doesn't make sense to me. You are stating that other studies have focused out several stated outcome and then you say this study addresses socio-demographic characteristics-this isn't an outcome. Are you trying to say that you considered socio-demographic characteristics in your assessment of outcomes?

Please clarify.

Sentence has been reworded.

28. Discussion- Future studies...may influence susceptibility to injury severity and injury proneness" why? For prevention purposes?

Sentence has been clarified.

29. Table 1. indicate what place of treatment other includes

This has been added in the methods section.

30. Table 1. Lots of data that isn't used/adjusted for in the paper-fine to show just commenting that some of this may contribute to the model. Numbers for previous adverse pregnancy outcomes would be a nice addition

One of our aims was to assess socio-demographic characteristics of injured and non-injured women. Some of these variables were not pertinent to the specific outcomes we assessed and therefore not included in the respective models, but were still of interest to the overall study.

31. Table 2-what is a vital activity?

A definition has been provided in a footnote.

32. Table 3-This table needs to be able to stand on its own.

Table has been modified.

33. Table 3. Neither the title or table notes that the ORs and HRs are adjusted and for what factors they are adjusted for.

Covariate names have been incorporated into the table.

34. Table 3 I would suggest changing abnormal to adverse in the title.

Changed.

35. Table 3 There needs to be labeling for which values are ORs and which are HRs and indication that there are 95% CIs.

Labeling has been added.

36. Table 3 References for the head/neck injuries and head injury calculations is not clear.

Clarifying statement has been added to the methods section.

VERSION 2 – REVIEW

REVIEWER	Erin K. Sauber-Schatz, PhD, MPH LCDR, US Public Health Service Senior Research Scientist Motor Vehicle Injury Prevention Team Division of Unintentional Injury Prevention National Center for Injury Prevention and Control, CDC, USA
REVIEW RETURNED	03/05/2012

THE STUDY	I suggest adding one more reference to the paper. Weiss HB, Sauber-Schatz EK, Cook LJ. Pregnancy-associated emergency department injury visits and their impact on birth outcomes. <i>Accid Anal Prev</i> 2008 May; 40(3); 1088-1095. should be added as a reference for the sentence “Adverse pregnancy outcomes resulting from maternal injury... in other studies [9-24].”
GENERAL COMMENTS	<p>I think the changes you made to the paper have made it much clearer and easier to read. Thank you for considering my comments and I think this will make a nice contribution to the literature. Below are a few remaining questions and minor editorial recommendations.</p> <p>Weiss HB, Sauber-Schatz EK, Cook LJ. Pregnancy-associated emergency department injury visits and their impact on birth outcomes. <i>Accid Anal Prev</i> 2008 May; 40(3); 1088-1095. Should be added as a reference for the sentence “Adverse pregnancy outcomes resulting from maternal injury... in other studies [9-24].”</p> <p>Methods</p> <ol style="list-style-type: none"> 1. I am still not clear what years of data from the DNBC were used. You say the cohort was established during 1996-2002 so are those the years of data you used for analysis? 2. There is still no comment on how many women had more than one birth during the study time period and if the authors have concerns and/or how they handled multiple births from the same woman within the data. <p>Results</p> <ol style="list-style-type: none"> 3. Insert the word “that” in the following statement “...table 3. We found that injured pregnant women were slightly more likely... or have pregnancies [that] were terminated by spontaneous abortion.” <p>Tables:</p> <ol style="list-style-type: none"> 4. Table 1 smoking status is 1-10 and ≥ 10 cigarettes a day? 5. Table 1 consider marking which comparisons were significantly

	<p>different more clearly in the table or adding a line of text about significant differences in the results section.</p> <p>6. To increase readability of Table 2 I suggest adding “N” as a label for the count column, adding percents to the table, and rank the description of injuries by frequency for each sub section (mode, activity etc.) while keeping other/unspecified last in each section.</p> <p>7. Table 3 is much easier to follow now. Just be consistent in your capitalization of the word “Reference”</p> <p>This paper doesn’t directly relate to your study, but just as an FYI for future work: Weiss, H., Sauber-Schatz, E. and Herring, A. (2011) Motor-vehicle crashes during pregnancy: a retrospective cohort study. Open Journal of Obstetrics and Gynecology, 1, 202-207. http://www.scirp.org/journal/PaperInformation.aspx?paperID=16486</p>
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VERSION 2 – AUTHOR RESPONSE

Response to Reviewers:

1. The 2008 paper by Weiss et al. has been added as a citation.
2. I am still not clear what years of data from the DNBC were used. You say the cohort was established during 1996-2002 so are those the years of data you used for analysis?
We have added clarification.
3. There is still no comment on how many women had more than one birth during the study time period and if the authors have concerns and/or how they handled multiple births from the same woman within the data.
Statement has been added to methods section.
4. Insert the word “that” in the following statement “...table 3. We found that injured pregnant women were slightly more likely... or have pregnancies [that] were terminated by spontaneous abortion.”
The word “that” has been included.
5. Table 1 smoking status is 1-10 and ≥ 10 cigarettes a day?
Yes.
6. Table 1 consider marking which comparisons were significantly different more clearly in the table or adding a line of text about significant differences in the results section.
Done.
7. To increase readability of Table 2 I suggest adding “N” as a label for the count column, adding percents to the table, and rank the description of injuries by frequency for each sub section (mode, activity etc.) while keeping other/unspecified last in each section.
Done.
8. Table 3 is much easier to follow now. Just be consistent in your capitalization of the word “Reference”
This has been noted.