ARTICLE DETAILS

TITLE (PROVISIONAL)	Pregnancy associated outcomes in women who spent some of their childhood looked after by local authorities: findings from the UK Millennium Cohort Study
AUTHORS	Botchway, Stella; Quigley, Maria; Gray, Ron

VERSION 1 - REVIEW

REVIEWER	Dr Fiona Mensah Murdoch Childrens Research Institute The Royal Children's Hospital Department of Pediatrics, University of Melbourne all Australia
REVIEW RETURNED	02-Jun-2014

| GENERAL COMMENTS | The manuscript is very well written, clear and accessible and adds important knowledge that is critical for the well being of this group of women and their families. The analyses are constructed effectively and address a clear rationale.

TITLE:
Is spending time 'in care' a term that will be understood internationally or does this need extra qualification.

INTRODUCTION:
Paragraph 3 suggests the potential for interventions to break the cycle of deprivation. It would be helpful to give some citation or suggestions of these and the context of their delivery. This is picked up on more in the discussion but I was left wondering what you had in mind at this stage.

Many of these women may have health and social vulnerabilities requiring extensive programs such as sustained home nurse visiting. It would be helpful to comment on this briefly in setting the context under which specific interventions to address smoking, depression and promote breastfeeding may be delivered.

It would be of interest to note research conducted by Professor John Hobcraft using 1958 British Birth Cohort. This research finds a high risk of adult outcomes indicative of social exclusion amongst women who spent time in care or foster care as children. The following web links provide a brief and link to the full report.
http://eprints.lse.ac.uk/51403/1/plugin-casebrief8.pdf
http://eprints.lse.ac.uk/6511/

METHOD:
The comparator group of mothers who did not experience time in care included those who had spent time in a prison or young |

offender's institution. These women may have similarly poor outcomes to the women who had spent time in care. I imagine this is a very small group of women and not likely to have had a large influence in the findings but would be good to consider a sensitivity analysis where these women are excluded from the comparator population.

In describing the socio-demographic characteristics of the population age at delivery is documented. This is very important as the risks of early child-bearing are high for women who have spent time in care. In the 1958 Birth cohort data presented by John Hobcraft (see above) the risk of teenage pregnancy is found to be high amongst women who have spent time in care or foster care as children.

I would suggest that it could be important in your work to also consider the women's age at their first birth as a very early first pregnancy can entail social risks that continue for subsequent later births. It is possible to derive age at first birth from the MCS data but requires a lot of coding to examine the household grid of family members as well as the questionnaire data about children no longer living in the home. I have Stata code that can derive this and would be happy to share this if applicable and you wanted to consider for this or future analyses.

Statistical analysis: paragraph 1, there is an error in the description of the classification of birth weight (both below 2.5kg) this is corrected in table 4.

Missing data: Women with missing data were excluded from the regression analyses. How many women were excluded for this reason? Did they differ from those who were included according to any information you have about these women? How would this have affected the results?

DISCUSSION:
The main limitation of the study is that the cohort may have excluded women who had themselves spent time in care and whose own children had been taken into care. This is acknowledged and is a widely found limitation of population level rather than specialist cohort studies. Please could you comment on how this is likely to have affected your findings in terms of the proportion of women in the population who are likely to have spent time in care and the strength of the risks they experience relative to women who have not spent time in care.

REVIEWER	Emily Harville
	Tulane University, United States
REVIEW RETURNED	15-Jul-2014

GENERAL COMMENTS	The authors present a large study of the relationship between being in care as a child and various maternal and child outcomes. Their results are unsurprising but add to the overall studies indicating long-term effects of childhood adversity on adult outcomes. There are limitations to their analysis, which the authors are aware of. I imagine the results are valid from an associational standpoint; whether they really demonstrate anything from a causal standpoint

could be argued.

Comments:

1. It is essentially impossible to separate the issues in the family of origin related to being in care vs. the effects of being in care.
2. Those who were in care were less likely to be recruited in and more likely to be lost to follow-up. There is probably differential attrition even within this group, with the most at-risk children most likely to be lost.
3. The women's experience of care necessarily happened 25 or so years ago. How have policies and societal trends shifted since then, and how might that affect the results?
4. What is the source of information for birthweight and gestational age?
5. The categorization for gestational age should be included in the methods.
6. Was their information on childhood SES? If not, this is a major potential confounder.
7. Choosing confounders based on statistical significance is not ideal; at the very least, the threshold for entry should be raised (0.20, for example). See: Maldonado G, Greenland S. Simulation study of confounder-selection strategies. Am J Epidemiol. 1993 Dec 1;138(11):923-36.
8. Choice of confounders is also difficult in this kind of analysis since many of the factors are potentially along the causal pathway. Being in care may make it more difficult to get a good education, for instance. The causal or explanatory models should be explained in more depth.
9. Do the authors have any explanation for the finding that women in care were less likely to have a c-section or instrumental delivery?
10. Given the high baseline prevalence of the outcomes, a log-binomial model should be considered. At the very least, interpreting the OR as a relative risk should be avoided. For instance, if 21% of the non-care participants smoked during pregnancy, it is impossible that 5 times as many care participants smoked.
11. The division between the outcomes in tables 3 and 4 is somewhat confusing. Table 5 includes outcomes from both. If birthweight is going to be emphasized in the abstract, a complete model should be provided for it, including potentially control for smoking, and gestational age should also be presented.

Reviewer 1 - Dr Fiona Mensah

1. Is spending time 'in care' a term that will be understood internationally or does this need extra qualification.

We agree that this term could be better explained in order to aid universal understanding. A more detailed description of care has been added to the manuscript. Unfortunately, terminology used to describe being 'in care' or 'looked after' varies due to national legislation, even within the devolved nations of the UK. We have used the coding and responses to the question 'have you ever lived outside the home' in the MCS to define what we mean by 'in care/looked after' in this study. The manuscript has been altered to make this clearer.

2. Paragraph 3 suggests the potential for interventions to break the cycle of deprivation. It would be helpful to give some citation or suggestions of these and the context of their delivery. This is picked up on more in the discussion but I was left wondering what you had in mind at this stage.

Further context for the delivery of interventions to improve the outcomes of pregnant women with social disadvantage has been added at this point, along with relevant references.

3. Many of these women may have health and social vulnerabilities requiring extensive programs such as sustained home nurse visiting. It would be helpful to comment on this briefly in setting the context under which specific interventions to address smoking, depression and promote breastfeeding may be delivered.

More information has been provided as suggested. See also the response to the comment above.

4. It would be of interest to note research conducted by Professor John Hobcraft using 1958 British Birth Cohort. This research finds a high risk of adult outcomes indicative of social exclusion amongst women who spent time in care or foster care as children. The following web links provide a brief and link to the full report.

http://eprints.lse.ac.uk/51403/1/plugin-casebrief8.pdf

http://eprints.lse.ac.uk/6511/

Thank you for drawing our attention to this important policy report, which we have now cited.

5. The comparator group of mothers who did not experience time in care included those who had spent time in a prison or young offender's institution. These women may have similarly poor outcomes to the women who had spent time in care. I imagine this is a very small group of women and not likely to have had a large influence in the findings but would be good to consider a sensitivity analysis where these women are excluded from the comparator population.

We looked again at mothers who had lived away from home for any reason. Only 2 out of 18,492 reported spending time in a prison or young offender's institution. Repeating the analyses with these women excluded did not change the findings.

7. I would suggest that it could be important in your work to also consider the women's age at their first birth as a very early first pregnancy can entail social risks that continue for subsequent later births. It is possible to derive age at first birth from the MCS data but requires a lot of coding to examine the household grid of family members as well as the questionnaire data about children no longer living in the home. I have Stata code that can derive this and would be happy to share this if applicable and you wanted to consider for this or future analyses.

Many thanks for offering to share this Stata code with us. We would be interested in looking at this variable in future analysis. We agree that age at first birth is an important variable, and some of this effect would have been captured by including mother's age at delivery in the model, although we recognise that this does not fully capture the effect expected by early first pregnancies. We have added sentence in the discussion which mentions this limitation.

8. Statistical analysis: paragraph 1, there is an error in the description of the classification of birth weight (both below 2.5kg) this is corrected in table 4.
This error has now been corrected.

9. Missing data: Women with missing data were excluded from the regression analyses. How many women were excluded for this reason? Did they differ from those who were included according to any information you have about these women? How would this have affected the results?
The number of women included in the analysis after the exclusion of women with missing data is presented in table 5. For the multivariable analysis of the outcome of smoking in pregnancy, 7 women were missing (0.04%), and for the outcome of breastfeeding, 4 women were missing (0.02%). We did not feel that this small number of missing would have affected the result as they were all from the unexposed group and not from the women who had been in care. For the outcome of symptoms of depression, 726 women were missing. Further analysis of these women was undertaken as suggested, and the results can be seen below, and are summarised in the manuscript.

Table s1. Women with data missing for the variable 'symptoms of depression'

	Women previously looked after	Women not previously looked after
Data on symptoms of depression	280	17,486
No data	11	715
% with missing data	3.9	4.0

Table s2. Characteristics of women previously been in care with missing data compared to those with data

Variable	% with data	% with missing data	P Value
Maternal age			0.6
<20	10.6	25.1	
20-29	59.5	53.6	
30-39	28.9	21.2	
>40	1.0	0	
Social class			0.2
Managerial	18.1	0	
Intermediate	16.2	10.5	
Routine	51.2	54.3	
Never worked	14.6	35.2	
Education			
Higher	12.2	0	0.5
Medium	7.4	10.8	
Lower	38.1	21.5	
Other	4.15	0	
None	38.1	67.7	
Household Income			0.6
<£10,400	47.3	75.2	
10,400-20,800	35.6	24.8	
£20,800 -31,200	9.9	0	
£31,200-52,000	5.5	0	
>£52,000	1.7	0	

Table s3. Characteristics of women not previously been in care with missing data compared to those

with data
Variable % with data % missing – women not in care P value
Maternal age <.001
<20 4.9 4.1
20-29 4.09 52.6
30-39 50.6 39.2
>40 3.6 4.2

Social class <0.001
Managerial 45.7 17.8
Intermediate 19.7 17.6
Routine 30.4 45.0
Never worked 4.2 19.6

Education <0.001
Higher 33.4 14.7
Medium 14.5 7.7
Lower 38.5 20.1
Other 2.1 13.2
None 11.6 44.3

Household Income <0.001
<£10,400 21.6 44.5
10,400-20,800 31.7 38.9
£20,800 -31,200 22.4 8.8
£31,200-52,000 17.4 3.4
>£52,000 7.0 4.5

10. The main limitation of the study is that the cohort may have excluded women who had themselves spent time in care and whose own children had been taken into care. This is acknowledged and is a widely found limitation of population level rather than specialist cohort studies. Please could you comment on how this is likely to have affected your findings in terms of the proportion of women in the population who are likely to have spent time in care and the strength of the risks they experience relative to women who have not spent time in care.
We agree that this is an important limitation, and as you point out we have acknowledged this is the manuscript. Given the minimal amount of literature investigating the experiences and outcomes of women who have been in care and who subsequently have children which they either keep or have taken into care also, it is difficult to go beyond speculation on how those who have children placed in the care system may differ to those who do not. However, we have added some speculative comments to the manuscript based on studies that look at the characteristics of families who have their children taken into care.
Reviewer 2 – Emily Harville

1. Those who were in care were less likely to be recruited in and more likely to be lost to follow-up. There is probably differential attrition even within this group, with the most at-risk children most likely to be lost.
This comment raises a similar point to comment 10 by reviewer 1. Please see response to comment 10 above.

2. The women's experience of care necessarily happened 25 or so years ago. How have policies and

societal trends shifted since then, and how might that affect the results?
Data from British birth cohorts from successive generations i.e the 1958, 1970 and 2000 cohorts show that children who have been in care consistently have worse health outcomes compared to their counterparts. However, direct comparison of the magnitude of effect has not been performed as far as we are aware. This would be an important piece of work to do in the future as successive policy attempts to redress this balance have highlighted failures in producing real change. As noted in the manuscript, there was an increased focus in the health and wellbeing of looked after children a decade or so ago. We have expanded our comments on this point following this comment.

4. What is the source of information for birth weight and gestational age?
Information for birth weight and gestational age was self reported in the questionnaire. However, some records in the the MCS are linked to hospital records, and previous studies have shown that there is a good correlation between self-report and hospital records for the items 'birth weight', 'gestational age' and 'mode of delivery', particularly in the categories used in this report. This information has been added to the manuscript.

5. The categorization for gestational age should be included in the methods.
This omission has been rectified.

6. Was their information on childhood SES? If not, this is a major potential confounder.
We agree that it would have been useful to consider this information as a potential confounder; however, unfortunately there is no information on the childhood socioeconomic class of the parents within the first sweep of the MCS. We also wonder whether, even if the data were available, would childhood SES would be a valid consideration for all children who had been in care, particularly those who spent a long time in care. It would be difficult to know whether the respondent was referring to their parents of birth or any subsequent foster or kinship parent, or responded with not applicable for the reasons that they were in care. We had added a note on this in the discussion of strengths and limitations of this study.

7. Choosing confounders based on statistical significance is not ideal; at the very least, the threshold for entry should be raised (0.20, for example). See: Maldonado G, Greenland S. Simulation study of confounder-selection strategies. Am J Epidemiol. 1993 Dec 1;138(11):923-36.
A plausible model was developed based on background literature. From our initial model, only ethnicity was subsequently removed as its inclusion did not have an appreciable effect on the result, and its removal appeared to make the model more robust. The wording in the manuscript has been changed slightly to make this process more apparent.

8. Choice of confounders is also difficult in this kind of analysis since many of the factors are potentially along the causal pathway. Being in care may make it more difficult to get a good education, for instance. The causal or explanatory models should be explained in more depth.
We agree with the reviewer that this is a difficulty when conducting studies in social epidemiology. In this paper we have not attempted to create a causal pathway, but to put forward possible associations between being in care and poor maternal outcomes based on background literature . We have added some possible examples of interplay between these associations to the manuscript .

9. Do the authors have any explanation for the finding that women in care were less likely to have a c-section or instrumental delivery?
We believe that this is because the women who had been in care were generally younger.

10. Given the high baseline prevalence of the outcomes, a log-binomial model should be considered. At the very least, interpreting the OR as a relative risk should be avoided. For instance, if 21% of the non-care participants smoked during pregnancy, it is impossible that 5 times as many care

participants smoked.
We appreciate these helpful comments of the reviewer and have adjusted our interpretation of the outcomes accordingly.

11. The division between the outcomes in tables 3 and 4 is somewhat confusing. Table 5 includes outcomes from both.
We attempted to divide the descriptive epidemiology into sociodemographic characteristics, pre-birth characteristics and post-birth characteristics in order to break up the results and avoid one long table. However, we appreciate that this is a personal preference, and although some readers may prefer small tables, others would wonder why this has been done. We have now combined table 3 and 4.

12. If birthweight is going to be emphasized in the abstract, a complete model should be provided for it, including potentially control for smoking, and gestational age should also be presented.
Birth weight was not been emphasised in the abstract. It was mentioned along with other key findings from our univariable analysis.

VERSION 2 – REVIEW

REVIEWER	Dr Fiona Mensah Murdoch Childrens Research Institute; Royal Children's Hospital; Department of Pediatrics, University of Melbourne; all Melbourne, Australia
REVIEW RETURNED	21-Aug-2014

GENERAL COMMENTS	Thank you for addressing the comments provided so comprehensively. I have detailed some further minor comments to follow. Methods: Symptoms of depression: please could it be clarified the period over which the instruments requests that mother's consider and report on their symptoms of depression (and anxiety?) Statistical analysis: where it is stated that the model appeared 'more robust', please could it be qualified what the authors mean, for example are the confidence intervals estimated with more precision for the estimates in the model? Discussion: Comparison with other studies: please could the final sentence 'It is likely that the families who were not recruited into the Millennium Cohort Study were more unstable than those who were, or who had a greater distrust of institutions.' be re-phrased. There are several meanings that could be taken from unstable so would be good to use a description which more closely indicates the types of instability families may be experiencing. Discussion: Comparison with other studies: paragraph 2: is elective caesarian also associated with higher socioeconomic position and resources? For typesetting: Abstract: 'Exposure A history of being a looked after a child' needs correction of the additional 'a'

	Methods: Potential confounding factors: extra quotation mark needed for 'A' level of equivalent.
	Statistical analysis: correction to 'mode fo delivery'
	Results: paragraph 3 - correction from 'achieve' to 'achieved'
	Discussion: Comparison with other studies: paragraph 2: correct 'a unassisted birth' to 'an'
	Conclusions: add 'are more' to 'as a looked after child disadvantaged socially'

REVIEWER	Emily Harville Tulane University, United States
REVIEW RETURNED	21-Aug-2014

GENERAL COMMENTS	I actually find 'in care' easier to understand than what the authors replaced it with, even though it is not a standard American expression. Perhaps it should just be defined initially and then the authors can revert to 'in care'. I would probably place in the information about missing data in the methods than the results, but that may be journal style. I would argue that including birthweight in the abstract and including a paragraph in the discussion constitutes emphasizing the birthweight results. Furthermore, I think these results are interesting – as interesting, in fact, as the behavioral and mental health, which I would have been extremely surprised to look any different. I would encourage the authors to present adjusted results for this outcome as well.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name Dr Fiona Mensah
Institution and Country Murdoch Childrens Research Institute;
Royal Children's Hospital;
Department of Pediatrics, University of Melbourne; all Melbourne, Australia
Please state any competing interests or state 'None declared': None declared

Dead Dr Botchway, Dr Quigley and Dr Gray,

Thank you for the opportunity to review this manuscript, and the critical contribution this knowledge this will make.

Thank you for addressing the comments provided so comprehensively.

I have detailed some further minor comments to follow.

Methods:
Symptoms of depression: please could it be clarified the period over which the instruments requests that mother's consider and report on their symptoms of depression (and anxiety?)

The following text has been added to the manuscript to provide additional detail on the Malaise Inventory: Symptoms of depression were measured using 9 questions of the validated Malaise Inventory [34], 'a tool used to within the Millennium Cohort Study to provide a measure of depression or psychological distress. It is a self-report tool phrased in plain language. There is no specified time frame over which participants are asked to report their symptoms, but the emphasis is on the recent past.'

Statistical analysis: where it is stated that the model appeared 'more robust', please could it be qualified what the authors mean, for example are the confidence intervals estimated with more precision for the estimates in the model?

The model without ethnicity had narrower confidence intervals and less missing data, despite the same odds ratio. This has been clarified in the text.

Discussion: Comparison with other studies: please could the final sentence 'It is likely that the families who were not recruited into the Millennium Cohort Study were more unstable than those who were, or who had a greater distrust of institutions.' be re-phrased. There are several meanings that could be taken from unstable so would be good to use a description which more closely indicates the types of instability families may be experiencing.
The main point we wanted to make was that families who have had their own children in care would have been excluded, which was made in the previous sentences. After reading your comment we felt that the sentence in question was superfluous, and so it was removed.

Discussion: Comparison with other studies: paragraph 2: is elective caesarian also associated with higher socioeconomic position and resources?

The evidence base is conflicting in regards to the relationship between caesarean section, and socioeconomic position and resources. Whilst some studies find an increased rate of caesarean section with deprivation measured at the area level (Barley, Aylin et al. 2004, Alves and Sheikh 2005), others find a more complicated relationship between age at first delivery, education, social class and mode of delivery, when individual level data are used. For example, primigravida women from a lower socioeconomic class having a higher rate of planned caesarean section or instrumental delivery (Essex, Green et al. 2013), whilst others still have found that individuals with a higher socioeconomic class have a higher rate of elective caesarean section, those with a lower socioeconomic class have a higher rate of emergency caesarean section (Fairley, Dundas et al. 2011). Education has also been associated with instrumental delivery, with a higher educational achievement being shown to be associated with a higher risk of planned caesarean section (Essex, Green et al. 2013). Given the conflicting previous research, we have only mentioned briefly these possible interactions in our manuscript in response to the reviewers comment.

For typesetting:
Abstract: 'Exposure A history of being a looked after a child' needs correction of the additional 'a'

Methods: Potential confounding factors: extra quotation mark needed for 'A' level of equivalent.

Statistical analysis: correction to 'mode fo delivery'

Results: paragraph 3 - correction from 'achieve' to 'achieved'

Discussion: Comparison with other studies: paragraph 2: correct 'a unassisted birth' to 'an'

Conclusions: add 'are more' to 'as a looked after child disadvantaged socially'

Many thanks for spotting these mistakes. A' Level has been changed to A Levels, as A' Level was the original way this exam was abbreviated (from the longer Advanced Level), but this presentation is less commonly used now compared to A Levels.

Reviewer: 2
Reviewer Name Emily Harville
Institution and Country Tulane University, United States
Please state any competing interests or state 'None declared': None declared

I actually find 'in care' easier to understand than what the authors replaced it with, even though it is not a standard American expression. Perhaps it should just be defined initially and then the authors can revert to 'in care'.
In care was changed in response to the previous comments of the first reviewer to make the terminology more easily understood. In the UK, 'in care' is a more informal reference to being in the care system, and reportedly more favoured than 'looked after' by children who have been in care themselves. However, it is more difficult to define. After reflecting the comments of both reviewers, a compromise has been attempted in the manuscript by creating a better description in the title and introduction/methods and then the use of 'in care' in other instances in the manuscript.

I would probably place in the information about missing data in the methods than the results, but that may be journal style.
The location of this information has been changed.

I would argue that including birthweight in the abstract and including a paragraph in the discussion constitutes emphasizing the birthweight results. Furthermore, I think these results are interesting – as interesting, in fact, as the behavioral and mental health, which I would have been extremely surprised to look any different. I would encourage the authors to present adjusted results for this outcome as well.
We have taken the encouraging advice of the reviewer and presented adjusted results for birth weight.
REFERENCES

Alves, B. and A. Sheikh (2005). "Investigating the relationship between affluence and elective caesarean sections." Bjog-an International Journal of Obstetrics and Gynaecology 112(7): 994-996.
Barley, K., P. Aylin, A. Bottle and B. Jarman (2004). "Social class and elective caesareans in the English NHS." BMJ 328(7453): 1399.
Essex, H. N., J. Green, H. Baston and K. E. Pickett (2013). "Which women are at an increased risk of a caesarean section or an instrumental vaginal birth in the UK: an exploration within the Millennium Cohort Study." BJOG: An International Journal of Obstetrics & Gynaecology 120(6): 732-743.
Fairley, L., R. Dundas and A. H. Leyland (2011). "The influence of both individual and area based socioeconomic status on temporal trends in Caesarean sections in Scotland 1980-2000." Bmc Public Health 11.