PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Childbirth, hospitalization, and sickness absence: a study of female twins
AUTHORS	Björkenstam, Emma; Alexanderson, Kristina; Narusyte, Jurgita; Kjeldgård, Linnea; Ropponen, Annina; Svedberg, Pia

VERSION 1 - REVIEW

REVIEWER	Giuseppe La Torre Sapienza University of Rome - Italy
REVIEW RETURNED	18-Oct-2014

GENERAL COMMENTS	- the abstract does not contain any figure in the results section. Add some relevant figure in terms of Hazard ratios and 95%CIs - explain in the methods section how the Cox proportional hazard assumptions are respected - add a sentence on the use of the STROBE statement in the methods section - in the results section, concerning the description of figure 2, the authors stated "Up to year T0, women who did not give birth had a higher average number of 244 hospitalization days and SA days compared to those who gave birth". Indicate in this sentence the mean values and 95%CIs bor both groups in the text, indicating also if these differences are significant or not.

REVIEWER	Ragnhild Elise Ørstavik Norwegian Institute of Public Health I am part of a Nordic collaboration on sick leave and disability research using twin cohorts, which includes the senior athors of this paper. We are currently applying for funding, and have so far not co-athorized any research papers.
REVIEW RETURNED	22-Oct-2014

GENERAL COMMENTS	Overall impression of the paper: This paper concerns the relationship between childbirth, hospitalization and sickness absence (SA) in female twins. In most countries with high labor force participation, women have substantially higher SA than men, and this gender difference is an important research field where the knowledge is still sparse. In my opinion, the current study adds valuable information to this field. The study applies high quality national registries and up to date statistical tools to address their research questions. The manuscript is well written. My main concern about this study is that it tries to address either too many or too broad a research question(s) at once, and thus becomes very difficult to interpret for the general

	reader. I have done my best to reflect this concern in the scoring of the paper and will explain my concerns in detail below: In the abstract, the authors state under aims that these are "to investigate associations of giving birth with morbidity in terms of hospitalization and social consequences of morbidity in terms of sickness absence (SA), while taking familial (genetics and shared environmental) factors into account". Then, in the Article Summary, the authors write that their focus is twofold: First, to address the association between giving birth with subsequent morbidity in terms of hospitality and SA and secondly, to study if hospitalization prior to (or after) childbirth increases the risk for future hospitalization and sickness absence. Much of the manuscript concerns this latter research question. In my opinion, this is confusing as it would be surprising if there was no association between being hospitalized (at any time point) and neither future hospitalization or SA. And, secondly, as exposure, the results from the cotwin control model when stratifying for hospitalization (usually applied to elucidate causal relationships) are less self-evident than those obtained when stratifying for giving birth. Whether there is a causal relationship between being hospitalized and later re-hospitalization or SA might be an interesting research question, but requires much explanation to the reader of a general medical journal, and should, in my opinion, not be included in the paper. In my view, the most interesting part of this publication is the possibility to elucidate the relationship between giving birth and SA. The authors correctly imply that SA is not a very good measure of morbidity. But as that applies to hospitalization as well (given that many common disorders and health problems do not require inpatient care), the data on hospitalization could better be used as an important covariate – either as a confounder (hospitalization prior to giving birth) or as a possible mediator (hospitalization in the years after giving birth), to explore to what degree the association (negative or positive) between giving birth and SA can be explained by morbidity in terms of hospitalization. The authors are correct in using the term "giving birth" throughout the paper, as this is neither sufficient nor necessary to raise a child. However, even though I am not familiar with the rates of adoption and stillbirth in Sweden, I would assume that the statistical errors due to stillbirth and adoption are limited, and that (other limitations taken into consideration) this paper is indeed very useful in exploring the double burden hypothesis (i.e. that women have higher rates of sick leave than men due to higher demands from household chores and childcare, again with the data on hospitalization as important covariates). It is correct that this hypothesis has been the subject of much research. This study is, however, the first to explore this research question applying the cotwin control design, and therefore an important contribution to this literature. The authors could be more confident in discussing how their results contribute to this hypothesis. That said, more information should be added on the details on the contents in the registries applied, and the strengths and limitations these provide. If, on the other hand, the authors wish to explore the relationship between actually giving birth and morbidity (then ideally adjusted for raising a child), this should be elaborated more in the introduction. Details: 1. This is a study on SA. As is explained on Page 12, lines 184-186, having income from work or unemployment benefits is a requirement for being eligible for SA in Sweden. Even though labor force participation is high, some information should thus be added about

	the employment status of the participants. If this is not possible, this should be mentioned in the limitations section. 2. More information should be added about the contents of the various registries: a. Swedish Birth Registry. Does the registry include all births (and abortions) regardless of gestational age? How many stillbirths were included in the current study? b. National Patient Register. Please specify early on whether this registry includes both inpatient and outpatient care. I read the article as only the former is included, but that should be specified early on in the paper. c. Swedish Twin Registry. Under Methods (page 10, first paragraph) the autors write that all twins born between 1959 and 1990 were included in the study. Please specify to what degree this represents all twins born during that time period (including e.g. immigrants), and if the registry is not complete, please say something on representativeness. 3. Page 8, line 115 and onwards. For a general medical journal, a short description of twins and the usefulness of twin studies should be included in the Introduction. I would prefer that this was elucidated so that a summary of what is now written in page 13, lines 216-228 is moved to the introduction. It is also a little confusing that “type of work” is described as a confounder that can be controlled for in twin studies (Page 9, line 123) as this is not the case. 4. Page 11, lines 180-182. "Number of women" is strictly not a measure but an outcome. I think what is meant here is "any new SA spell between years 2-5 (yes/now)”. Please specify. 5. Page 12, lines 195-197. This is a rather young sample, the overall educational level in Sweden is high, and as evident from Table 1 this also applies to the current sample. In many societies, there is a strong correlation between educational level and age of giving birth to one’s first child, as well as health and SA. I would therefore prefer that this important confounder was stratified into four instead of three categories (adding a category of higher university level). More importantly, some information on the relationship between educational level and age at giving birth should be included in the paper. 6. Page 13, lines 216-228. Readers of a general medical journal are not familiar with twin studies and the cotwin control design. This paragraph should therefore be moved to the introduction. 7. Lines 236-237. The difference in hospitalization between the two groups was very small and in favor of those not giving birth. This does not support a hypothesis of health selection Into giving birth. Please also specify how the numbers referred in the text corresponds to those given in the table. 8. Page 19, last paragraph: The authors conclude that their study does not support that giving birth is associated with future health problems (line 326). They then state, without reference, that giving birth is in itself a risk factor for future morbidity. Please clarify. 9. Page 20, second paragraph (lines 341-9). Here the authors discuss the finding that hospitalization (either before or after) giving birth predicts future SA, and that this association is stronger among women with recurrent hospitalizations. This is not surprising. However, they then state that such an association has been questioned. Although I am not familiar with the details in this reference, I strongly doubt that anyone would suggest that there is no association between morbidity and SA (in any population). The discussion is more in the direction of to what degree morbidity explains SA, or differences in SA in different groups. Please specify.

	10. Limitations section: As the authors write, data on hospitalization are far from ideally suited to explore morbidity. The registry data available for this study is probably unique and should be recognized as such. Nevertheless, the most important measures of morbidity in this age group would probably be data from general practitioners and outpatient clinics. This should be mentioned in the limitations section. The same applies to the lack of diagnoses underlying the SA spells, especially as SA due to pregnancy related disorders cannot be excluded from the analyses. It is also worth emphasizing that only SA spells exceeding 10 days are included in the limitations section, and, in the same line, avoiding the expression "1 day" in the column heading of the tables. 11. Table 1, column 2, line 16. 21% must be wrong. 12. Table 1, column 21. Should be >40, not <40 13. Table 2, 3 and 4 are difficult to understand without reading the text. Par example, it is not obvious from the table itself the difference between the groups listed in line 13 and 19 (or 14 and 20).

VERSION 1 – AUTHOR RESPONSE

Reviewer #1:
The abstract does not contain any figure in the results section. Add some relevant figure in terms of Hazard ratios and 95%CIs
Reply: We acknowledge this suggestion and have added relevant figures to the abstract
Changes in manuscript: Page 2, lines 39-41

Explain in the methods section how the Cox proportional hazard assumptions are respected
Reply: A sentence about this was added to the Methods section.
Changes in manuscript: Page 11, lines 274-276.

Add a sentence on the use of the STROBE statement in the methods section
Reply: As suggested, we have added a sentence in the Methods section.
Changes in manuscript: Page 11, line 278.

In the results section, concerning the description of figure 2, the authors stated "Up to year T0, women who did not give birth had a higher average number of 244 hospitalization days and SA days compared to those who gave birth". Indicate in this sentence the mean values and 95%CIs for both groups in the text, indicating also if these differences are significant or not.
Reply: We have now added information stating the mean values and clarifying the differences between the groups.
Changes in manuscript: Page 12, lines 324-330.

Reviewer #2:
Comments to authors

Overall impression of the paper:
This paper concerns the relationship between childbirth, hospitalization and sickness absence (SA) in female twins. In most countries with high labor force participation, women have substantially higher SA than men, and this gender difference is an important research field where the knowledge is still sparse. In my opinion, the current study adds valuable information to this field.
The study applies high quality national registries and up to date statistical tools to address their research questions. The manuscript is well written. My main concern about this study is that it tries to address either too many or too broad a research question(s) at once, and thus becomes very difficult to interpret for the general reader. I have done my best to reflect this concern in the scoring of the paper and will explain my concerns in detail below:

In the abstract, the authors state under aims that these are “to investigate associations of giving birth with morbidity in terms of hospitalization and social consequences of morbidity in terms of sickness absence (SA), while taking familial (genetics and shared environmental) factors into account”. Then, in the Article Summary, the authors write that their focus is twofold: First, to address the association between giving birth with subsequent morbidity in terms of hospitality and SA and secondly, to study if hospitalization prior to (or after) childbirth increases the risk for future hospitalization and sickness absence. Much of the manuscript concerns this latter research question. In my opinion, this is confusing as it would be surprising if there was no association between being hospitalized (at any time point) and neither future hospitalization or SA.
Reply: We agree with the reviewer, indeed it would have been surprising if there was no association at all between hospitalization and SA; however, there are hardly any published studies on this. Moreover, often the level of morbidity in sickness absent mothers often is questioned, e.g. in media and the political discussions– it is rather assumed that they are sickness absent to care for their children or other domestic chores. We agree that these issues are complex and in that we might not have been consistent in how the aims were put forth; hence, we have rephrased the aim in the article summary and in the manuscript text, in line with the abstract in order to be consistent.
Changes in manuscript: See pages 4 and 7.

And, secondly, as exposure, the results from the cotwin control model when stratifying for hospitalization (usually applied to elucidate causal relationships) are less self-evident than those obtained when stratifying for giving birth. Whether there is a causal relationship between being hospitalized and later re-hospitalization or SA might be an interesting research question, but requires much explanation to the reader of a general medical journal, and should, in my opinion, not be included in the paper.
Reply: You are right in that we have elucidated many different questions in this study. The unique twin data provides this possibility and others might rather wonder, or even suspiciously question, if we had not included those analyses when having access to those special types of data. This would not be possible to study with other types of data.

In my view, the most interesting part of this publication is the possibility to elucidate the relationship between giving birth and SA. The authors correctly imply that SA is not a very good measure of morbidity. But as that applies to hospitalization as well (given that many common disorders and health problems do not require inpatient care), the data on hospitalization could better be used as an important covariate – either as a confounder (hospitalization prior to giving birth) or as a possible mediator (hospitalization in the years after giving birth), to explore to what degree the association (negative or positive) between giving birth and SA can be explained by morbidity in terms of hospitalization.
Reply: We agree and hospitalization prior to delivery was also included as a confounder in the analyses in the 3rd step. The analytical steps are described in the method section.
Changes in manuscript: See page 11 and table 3

The authors are correct in using the term "giving birth" throughout the paper, as this is neither sufficient nor necessary to raise a child. However, even though I am not familiar with the rates of adoption and stillbirth in Sweden, I would assume that the statistical errors due to stillbirth and adoption are limited, and that (other limitations taken into consideration) this paper is indeed very useful in exploring the double burden hypothesis (i.e. that women have higher rates of sick leave than men due to higher demands from household chores and childcare, again with the data on hospitalization as important covariates). It is correct that this hypothesis has been the subject of much research. This study is, however, the first to explore this research question applying the cotwin control design, and therefore an important contribution to this literature. The authors could be more confident in discussing how their results contribute to this hypothesis. That said, more information should be added on the details on the contents in the registries applied, and the strengths and limitations these provide.
If, on the other hand, the authors wish to explore the relationship between actually giving birth and morbidity (then ideally adjusted for raising a child), this should be elaborated more in the introduction.
Reply: As you state, there are great overlaps between giving birth and raising a child. Nevertheless, some women who did not give birth still live with children – through adoption or moving in with a partner who has children in a previous relationship. Some women who give birth to a living child do not live with the child, due to different reasons. You are right in assuming that our aim here was to focus on having given birth or not. There has been discussions for several years in Sweden regarding whether giving birth involves any medical risks – assuming it does not, and therefore there should be no associations with this and SA. The aim of this study – the first ever of its kind – was to elucidate some aspects of this. Of course several other studies, e.g., according to your suggestions, should be conducted. We hope that this study will be a starting point for other such studies.

Details:
1. This is a study on SA. As is explained on Page 12, lines 184-186, having income from work or unemployment benefits is a requirement for being eligible for SA in Sweden. Even though labor force participation is high, some information should thus be added about the employment status of the participants. If this is not possible, this should be mentioned in the limitations section.
Reply: We agree that this is important information and we have now added data on labor force participation. As explained in the text, also women with unemployment benefits, parental benefits and students can be sickness absent with benefits - that is the reason for why we initially did not include specific numbers on this.
Changes in manuscript: See addition on page 8 (participants) regarding percentage of the sample who were employed, on unemployment benefits, or students in the year prior to the birth year (i.e. T-1).

2. More information should be added about the contents of the various registries:
a. Swedish Birth Registry. Does the registry include all births (and abortions) regardless of gestational age? How many stillbirths were included in the current study?
Reply: We acknowledge this suggestion, and we have added further description about the registers to the methods section. Regarding the Medical Birth Register, stillbirths are included in the register – all births, irrespective if the child lived or not, are included in the analyses.
Changes in manuscript: See page 8, method section.

b. National Patient Register. Please specify early on whether this registry includes both inpatient and outpatient care. I read the article as only the former is included, but that should be specified early on in the paper.
Reply: Only inpatient care was considered in this study and referred to as hospitalizations throughout the manuscript. We acknowledge that outpatient data would have been useful, but unfortunately we did not have access to such data. Also, the Swedish outpatient register did not start until 2001, and thus it would not have been useful with such data in this study.

Changes in manuscript: See addition regarding NPR and inpatient data on page 8-9.

c. Swedish Twin Registry. Under Methods (page 10, first paragraph) the authors write that all twins born between 1959 and 1990 were included in the study. Please specify to what degree this represents all twins born during that time period (including e.g. immigrants), and if the registry is not complete, please say something on representativeness.
Reply: The Swedish Twin Registry (STR) contains all twin births in Sweden; hence, twins not born in Sweden are not included in STR and as a consequence, external validity might be lower to women born outside Sweden.
Changes in manuscript: We have added a sentence on external validity in the limitation paragraph on page 19.

3. Page 8, line 115 and onwards. For a general medical journal, a short description of twins and the usefulness of twin studies should be included in the Introduction. I would prefer that this was elucidated so that a summary of what is now written in page 13, lines 216-228 is moved to the introduction. It is also a little confusing that "type of work" is described as a confounder that can be controlled for in twin studies (Page 9, line 123) as this is not the case.
Reply: The text in question on in the methods section has been moved to the introduction. section. The text on 'type of work' has now been deleted.
Changes in manuscript: As suggested most of the text in the method section regarding the benefits of using a twin setting was moved to the introduction, see page 7.

4. Page 11, lines 180-182. "Number of women" is strictly not a measure but an outcome. I think what is meant here is "any new SA spell between years 3-5 (yes/now)". Please specify.
Reply: As suggested we have made these changes in the manuscript.
Changes in manuscript: See page 10, lines 226-227.

5. Page 12, lines 195-197. This is a rather young sample, the overall educational level in Sweden is high, and as evident from Table 1 this also applies to the current sample. In many societies, there is a strong correlation between educational level and age of giving birth to one's first child, as well as health and SA. I would therefore prefer that this important confounder was stratified into four instead of three categories (adding a category of higher university level). More importantly, some information on the relationship between educational level and age at giving birth should be included in the paper.
Reply: Thank you for this comment. To clarify we have added rationales as to why educational level was considered a potential confounder, in the methods section. We have also added two references to this. We appreciate your suggestion regarding stratifying educational level even more, however, even three levels are much, regarding the limited numbers, why we prefer to keep three categories.
Changes in manuscript: See page 10, lines 241-243.

6. Page 13, lines 216-228. Readers of a general medical journal are not familiar with twin studies and the cotwin control design. This paragraph should therefore be moved to the introduction.
Reply: The text in the methods section has been moved to the introduction section as suggested.
Changes in manuscript: See page 7.

7. Lines 236-237. The difference in hospitalization between the two groups was very small and in favor of those not giving birth. This does not support a hypothesis of health selection into giving birth. Please also specify how the numbers referred in the text corresponds to those given in the table.
Reply: The 30% was obtained by summarizing 1,183 (both gave birth) and 407 (one in pair gave birth) those that had at least one hospitalization during the period six years prior through six years after T0 (excluding hospitalizations with a diagnosis for pregnancy and childbirth), and dividing this number with 5,118. We have added text to specify these numbers.
Changes in manuscript: See page 12 lines 315-316.

8.Page 19, last paragraph: The authors conclude that their study does not support that giving birth is associated with future health problems (line 326). They then state, without reference, that giving birth is in itself a risk factor for future morbidity. Please clarify.
Reply: Please note, we conclude that giving birth is not associated with future hospitalization nor with future SA. We have no other information about future health problems. In order to clarify, we added references to this statement.
Changes in manuscript: See page 16, line 421 (ref. 16, 19, 22)

9. Page 20, second paragraph (lines 341-9). Here the authors discuss the finding that hospitalization (either before or after) giving birth predicts future SA, and that this association is stronger among women with recurrent hospitalizations. This is not surprising. However, they then state that such an association has been questioned. Although I am not familiar with the details in this reference, I strongly doubt that anyone would suggest that there is no association between morbidity and SA (in any population). The discussion is more in the direction of to what degree morbidity explains SA, or differences in SA in different groups. Please specify.
Reply: Thank you for this comment, making it obvious to us that we had not been clear enough in our discussion. There are hardly any studies on the association between morbidity, e.g., in terms of hospitalization, and SA. Instead, in the general political discussions and in the mass media, it is often a question whether women with children that are on SA actually have morbidity or are on SA due to other reasons – e.g., to care for domestic tasks. It is also stated that giving birth is not associated with any type of risks of morbidity. In this study we have studied associations of morbidity with SA, both among women giving birth and not giving birth.
Changes in manuscript: None.

10.Limitations section: As the authors write, data on hospitalization are far from ideally suited to explore morbidity. The registry data available for this study is probably unique and should be recognized as such. Nevertheless, the most important measures of morbidity in this age group would probably be data from general practitioners and outpatient clinics. This should be mentioned in the limitations section. The same applies to the lack of diagnoses underlying the SA spells, especially as SA due to pregnancy related disorders cannot be excluded from the analyses. It is also worth emphasizing that only SA spells exceeding 10 days are included in the limitations section, and, in the same line, avoiding the expression "1 day" in the column heading of the tables.
Reply: We agree that this is as a limitation, and we now have stressed this further in the limitation section. The strength of 'only' having in-patient data is that this means we included the more severe morbidity. We also agree that it would have added having knowledge on the sick-leave diagnoses. Nevertheless, we in a study on data from the 1980's showed that about half of the sickness absence among pregnant women did not reveal information on the state of pregnancy or if the sick-leave diagnosis was pregnancy related. We have included that the lack of information on the shorter sick-leave spells is a limitation.
Changes in manuscript: Page 18, lines 466-471.

11. Table 1, column 2, line 16. 21% must be wrong.
Reply: Thank you for pointing this out, it has now been corrected to 2%.
Changes in manuscript: Page 25
12. Table 1, column 21. Should be >40, not <40
Reply: Thank you, this has now been corrected.
Changes in manuscript: Page 24

13. Table 2, 3 and 4 are difficult to understand without reading the text. Par example, it is not obvious from the table itself the difference between the groups listed in line 13 and 19 (or 14 and 20).
Reply: Thanks for pointing out that we were unclear about this. We have now added information in the

different tables.
Changes in manuscript: Page 25-27

VERSION 2 – REVIEW

REVIEWER	Giuseppe La Torre Sapienza University of Rome Italy
REVIEW RETURNED	24-Nov-2014

GENERAL COMMENTS	The authors made the requested amendments and now the manuscript is suitable for publication on the journal

REVIEWER	Ragnhild Elise Ørstavik Norwegian Institute of Public Health, Norway I am part of a Nordic collaboration on sick leave and disability research using twin cohorts, which includes the senior athors of this paper. We are currently applying for funding, and have so far not co-athorized any research papers.
REVIEW RETURNED	10-Dec-2014

GENERAL COMMENTS	Thanks for your response to my review. The paper has improved and is, in my view, an important contribution to understanding health and sickness absence among women. I have now only one concern/request. I am not sure if readers of a general medical journal, especially readers from countries outside Scandinavia, will fully understand that there have been speculations about whether there is a link between health and sick leave in women. Even though the aims of the study have been rephrased, the association between morbidity and SA is still included in the introduction and discussion section. In my opinion, the manuscript would benefit from a few more sentences (and, ideally, references) explaining why exploring the causal link between morbidity and sick leave is important in this particular population. Otherwise, I am very satisfied with the revision.

VERSION 2 – AUTHOR RESPONSE

Reviewer #2:
Comments to authors
I have now only one concern/request. I am not sure if readers of a general medical journal, especially readers from countries outside Scandinavia, will fully understand that there have been speculations about whether there is a link between health and sick leave in women. Even though the aims of the study have been rephrased, the association between morbidity and SA is still included in the introduction and discussion section. In my opinion, the manuscript would benefit from a few more sentences (and, ideally, references) explaining why exploring the causal link between morbidity and sick leave is important in this particular population.
Reply: We have added a few sentences and three references to the introduction section.
Changes in manuscript: Page 6, lines 113-115.