## PEER REVIEW HISTORY

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## **ARTICLE DETAILS**

TITLE (PROVISIONAL)	Sick leave and medication use in pregnancy - a European web- based study
AUTHORS	Truong, Bich; Lupattelli, Angela; Kristensen, Petter; Nordeng, Hedvig

# **VERSION 1 - REVIEW**

REVIEWER	M van Poppel Institute of Sport Science, University of Graz, Graz, Austria
REVIEW RETURNED	22-Feb-2017

GENERAL COMMENTS	Sick leave and medication use in pregnancy - a European web- based study	
	The paper addresses the topic of sick leave in pregnancy, taking in account medication use and different sick leave schemes. Sick leave in pregnancy is a relevant topic, since the contribution of women to the work force is large and still increasing. Keeping women healthy during and after pregnancy therefore has societal and economic relevance. To date, no multinational studies on this topic are available, which limits our understanding of factors associated with sick leave in pregnancy. The paper is in general well written.	
	Major comments:	
	I have some difficulties understanding the analyses conducted and interpreting the results. This is most clearly demonstrated with the results presented in Table 3:	
	- The first independent variable is 'medication use for chronic conditions'. From the results presented it seems that, after adjustment, this variable is not related to the risk of sick leave during pregnancy, or having extended sick leave. This is for me a remarkable finding, that should be mentioned and addressed in the paper, when correct. However, when I read the footnote correctly, this model is adjusted for the variable 'chronic conditions'. I don't think this is the correct way to analyse these data and would prefer doing it similar to the other independent variables (condition not present, present but not medicated, present and medicated).	

- I would suggest using the same set of confounders for all analyses, this makes it easier to read and understand and will probably not make much of a difference. If it DOES make a relevant difference, I would be worried about the robustness of the findings.
- For such a standard set of confounders, please rethink which factors may or may not be included. I am not sure whether adjusting for acute health conditions is possible when looking at one of those conditions as the independent variable (similar problem as above with the chronic conditions). Looking at the differences between the crude and adjusted ORs, I believe that there are differences in sick leave between women with non-medicated conditions versus women without those conditions, which obviously disappear when adjusting for having an acute health condition.
- How much overlap is there between women having NVP and/or pain and/or sleeping problems? From Table 2, it seems there is considerable overlap! And as I understand Table 3, all these variables have been studied in separate models and not as different variables in the same model. What would result from a model in which all three acute health problems are entered simultaneously? It might give an indication of the relative importance of these conditions to sick leave in pregnancy.

Another major concern that I have with the paper, is that differences in maternity leave are not considered very much, although this topic is addressed in the discussion. The authors differentiated between countries with high, medium and low sick leave schemes, but not between countries with long/short/no maternity leave before giving birth. I do believe (as they also indicated in the discussion) that this influences whether women report sick leave or not very much. Would it be possible to combine the sick leave schemes with maternity leave schemes? Or at least look at differences in sick leave in the first trimester only as a sensitivity analyses, since so early in pregnancy women will not be on maternity leave?

Lastly, although it is interesting to look at women with and without medication, I would focus the paper more around sick leave of women with or without certain health conditions. I believe that has more relevance for occupational and public health at the moment.

More discussion around how the results of this study can be used in improving work and/or health care of pregnant women, or reducing sick leave is also warranted in the paper.

### Minor comments:

• Line 57, page 4: "Furthermore, none of the previous studies ....." this sentence can be deleted, since almost a duplicate of lines

	10-11 on page 5.
•	Multiple sick leave is used in several places, and in others
	extension of sick leave. Please use the last consistently.
•	Page 7, lines 39-40: why did the authors focus on NVP, pain
	and sleeping problems only? Some justification for this choice is needed.
•	Page 13 and 14: is discussing the differences between
	medications really relevant for the paper? It is a bit distracting, and makes a complicated paper even more complicated.
	Table 2: adding the % of medicated and non-medicated women
	in the column with Total would be helpful.
•	Page 14, line 18: "Women from countries with "High" sick leave
	schemes had the" Since this was only Norway, perhaps best
	rephrase as: "Women from Norway with a "High" sick leave
	scheme had the"
•	Page 14, line45: than the one observed in the main analysis and <b>were</b> no longer significant. Delete 'were'. Next line:
	medication use was no longer significant, but did the magnitude
	of the association change as well?
•	Page 18, line 4: could affect sick leave rates, distinguishing these sectors could have (delete 'a' and 'of'
•	Page 18, line 23: shown instead of showed.
•	Page 18, line 50: again also describe if the magnitude of the
	associations changed, not only the significance, since the last is most influenced by sample size.
	Supplementary figure 1: it is 'The Netherlands', and not 'The
	Nederland'.
•	References: I believe more recent studies are available on sick
	leave in pregnancy that might be relevant for the discussion
	(e.g. Hansen ML, Thulstrup AM, Juhl M, et al. Predictors of
	sickness absence in pregnancy: a Danish cohort study. Scand J Work Environ Health 2015;41(2):184-93)

REVIEWER	Stefan Malmqvist Department of Health Studies University of Stavanger Norway
REVIEW RETURNED	14-Apr-2017

GENERAL COMMENTS	An interesting and well-prepared article.

# **VERSION 1 – AUTHOR RESPONSE**

# Response to the reviewer's comments to the authors

We thank the reviewers for their feedback and constructive and helpful comments on our manuscript "Sick leave in pregnancy – a European web-based study". We have tried to address and

implement in the revised version of the manuscript all comments and remarks. All changes to the original manuscript have been marked by using red text color. The original manuscript has also been thoroughly checked for typographical/grammatical errors as recommended.

#### Reviewer 2:

The paper addresses the topic of sick leave in pregnancy, taken into account medication use and different sick leave schemes. Sick leave in pregnancy is a relevant topic, since the contribution of women to the work force is large and still increasing. Keeping women healthy during and after pregnancy therefore has societal and economic relevance. To date, no multinational studies on this topic are available, which limits our understanding of factors associated with sick leave in pregnancy. The paper is in general well written.

## Major comment 1:

The first independent variable is "medication use for chronic conditions". From the results presented it seems that, after adjustment, this variable is not related to the risk of sick leave during pregnancy, or having extended sick leave. This is for me a remarkable finding that should be mentioned and addressed in the paper, when correct. However, when I read the footnote correctly, this model is adjusted for the variable "chronic conditions". I don't think this is the correct way to analyze these data and would prefer doing it similar to the other independent variables (condition not present, present but not medicated, present and medicated).

#### Reply 1:

Thank you for this important remark. The main objective of our study was to investigate whether maternal medication use in pregnancy was associated with sick leave during pregnancy. Since our models are based on "Medication use" as the exposure and "Sick leave" as the outcome, it seemed necessary to adjust for the maternal underlying condition; indeed, the maternal underlying condition is a common cause of both medication use and sick leave in pregnancy, and thus a confounding factor on this association (see Figure 1 in Reply 2).

However, we do agree with the reviewer that grouping all the chronic conditions is not ideal, and contrasting medicated versus non-medicated chronic disorders in relation to sick leave would add to our current knowledge. We have now done all analyses on the four most prevalent chronic conditions in pregnancy: i) mood disorders (i.e., depression and anxiety), ii) asthma, iii) allergy, and iv) hypothyroidism, categorized as suggested (condition not present, present but not medicated, present and medicated). The Method section has been updated with the following text: "The four most prevalent chronic conditions were also studied, i.e. mood disorders (depression and anxiety), asthma, allergy, and hypothyroidism".

The results have been added in Table 3 in the manuscript and show that treatment of different chronic disorders impact differently on sick leave rates. Most importantly, women with mood disorders requiring pharmacotherapy had a two to three fold increased likelihood of sick leave in pregnancy compared with their counterparts. Medication use might in fact be a marker of severity of mood disorder, explaining the higher sick leave rates. On the other hand, we see that women with non-medicated somatic chronic disorders had higher likelihood of being on sick leave. For these women, under treatment and non-adherence<sup>1</sup> might be factors enhancing sick leave rates. The amended text in the Results section now reads: "Having chronic asthma, allergy, hypothyroidism, or mood disorders was positively associated with sick leave in pregnancy regardless of medication use (Table 3). Women who did not report any treatment (non-medicated) for asthma, allergy, and hypothyroidism had a higher likelihood (1.5-2.7-fold) of being on sick leave compared with women without the disorder. These associations were greater than for medicated women (1.3-1.5-fold), whereas, the inverse was observed in relation to mood disorders (non-medicated vs. medicated OR: 2.1 vs. 3.1).

The association between medicated acute illnesses and sick leave was also greater than for non-medicated illnesses and sick leave, when compared with no acute illness (Table 3)".

We have now discussed more thoroughly these findings, and amended the Discussion section as follows: "The association between non-medicated chronic disorders (i.e., asthma, allergy, and hypothyroidism) and sick leave was greater than the association for medicated chronic disorders, when both groups were compared with women having no chronic disorder. Yet, the opposite trend was seen for all the acute illnesses investigated as well as for chronic mood disorders. .... Indeed, pharmacological treatment with antidepressants in pregnancy is usually reserved for women with a major mood disorder, or as a second line therapy when non-pharmacological therapies have failed.<sup>2</sup> Thus, medication use for acute illnesses as well as for mood disorders may be a proxy for the severity of the conditions. However, studies have shown that common pregnancy-related illnesses, such as NVP, are often mismanaged and neglected by health care personnel.<sup>3</sup> The results of our study may support these findings as the magnitude of the association between non-medicated and medicated acute illnesses, specifically for NVP and sleeping problems, was greater than that for chronic disorders. Reducing sick leave rates among pregnant women is beneficial for public health, and has major economic interest for society. Previous research has mainly focused on preexisting chronic disorders in pregnancy, and these women are generally followed-up adequately. However, our study indicates there is a need to focus on other aspects in pregnancy. Therefore, future research should investigate whether or not sick leave among pregnant women can be prevented by optimizing management of acute pregnancy-related illnesses".

#### Major comment 2:

I would suggest using the same set of confounders for all analysis, this makes it easier to read and understand and will probably not make such of a difference. If it DOES make a relevant difference, I would be worried about the robustness of the findings.

### Reply 2:

Thank you for this comment. The selection of confounding variables is now based on prior knowledge and current literature, by using Direct Acyclic Graph. All analyses have now been adjusted for the same set of confounders, e.g. sociodemographic variables, chronic conditions, acute conditions, smoking, alcohol, and health-related variables (Figure 1). We have now amended the Methods section. Specifically the following text has been added: "Potential confounders were identified according to prior knowledge and current literature, and by using Direct Acyclic Graphs. The same set of confounders (i.e. maternal age, parity, maternal status, marital status, education level, employment, infertility treatment, whether or not the pregnancy was planned, alcohol use in pregnancy, smoking in pregnancy, acute conditions [others than the one of interest], and chronic disorders [others than the one of interest], was used for all models containing medication use as the independent variable".

Our point estimates adjusted for the same set of confounders, did not materially change from our original results.

Sociodemographic variables

Chronic condition

Acute condition

Medication use

Smoking

Alcohol

Health-related variables

**Figure 1:** Simplified conceptual graph visualizing the relationship between "Medication use", "Sick leave", and potential confounders.

Since there is scarce information about factors related to "Sick leave policy", and thus drawing a DAG is challenging; the selection of confounding variables pertaining to the association between "Sick leave policy" and sick leave in pregnancy was and is still based on impact on the beta coefficients for "Sick leave policy" (as described in the Methods). Therefore, no change has been done in relation to this analysis. However, to enhance clarity, we have now presented the results on sick leave schemes in the text, and omitted them from Table 3 in the manuscript.

### Major comment 3:

For such a standard set of confounders, please rethink which factors may or may not be included. I am not sure whether adjusting for acute health conditions is possible when looking at one of those conditions as the independent variable (similar problem as above with the chronic conditions). Looking at the differences between the crude and adjusted ORs, I believe that there are differences in sick leave between women with non-medicated conditions versus women without those conditions, which obviously disappear when adjusting for having an acute health condition.

### Reply 3:

Thank you for this comment. We have now used the same set of confounders for all analyses containing medication use as the independent variable as described in Reply 2. The only difference is that we have not adjusted for the condition of interest, but for all other conditions. For instance, the model including "Nausea and vomiting in pregnancy" as the independent variable has now been adjusted for all other acute conditions and chronic conditions but NOT for nausea and vomiting. The same applies to all other models with medication use as the independent variable. As presented in Table 3 in the manuscript, the results did not materially differ from the ones stemming from the original analyses.

### Major comment 4:

How much overlap is there between women having NVP and/or pain and/or sleeping problems? From Table 2, it seems there is considerable overlap! And as I understand Table 3, all these variables have been studied in separate models and not as different variables in the model. What would result from a model in which all three acute health problems are entered simultaneously? It might give an indication of the relative importance of these conditions to sick leave in pregnancy.

#### Reply 4:

There is a considerable overlap between women having NVP and/or pain and/or sleeping problems. As shown in Table 1 below, almost half of the women did have all three conditions. However, as addressed in our previous responses, the models are now adjusted for all other acute conditions, except the one under study.

**Table 1:** Number of acute conditions (NVP and/or pain and/or sleeping problems).

Number of acute conditions  (NVP and/or pain and/or sleeping problems)	<b>n</b> (%, n=6.686)
0	478 (7.2)
1	1.406 (21.0)
2	2.032 (30.4)
3	2.770 (41.4)

#### Major comment 5:

Another major concern that I have with the paper, is that differences in maternity leave are not considered very much, although this topic is addressed in the discussion. The authors differentiated between countries with high, medium and low sick leave schemes, but not between countries with long/short/no maternity leave before giving birth. I do believe (as they also indicated in the discussion) that this influences whether women report sick leave or not very much. Would it be possible to combine the sick leave schemes with maternity leave schemes? Or at least look at differences in sick

leave in the first trimester only as a sensitivity analysis, since so early in pregnancy women will not be on maternity leave?

#### Reply 5:

Thank you for this remark. We have now tried to consider the differences in maternity leave in each country by doing sensitivity analyses restricted to pregnant women (not new mothers) who were not qualified to receive maternity leave as presented in Table 2 below. We used the reported week of gestation when the electronic questionnaire was completed for this purpose. We adopted a restrictive approach regarding the time period in which maternity leave can be taken in each country. E.g. in Croatia, pregnant women are in general qualified for maternity leave 28 days before the expected date of birth, but the maternity leave can be taken up to 45 days prior if there are complications resulting from the pregnancy. We have used 45 days as the cut-off for Croatia in these analyses. The following text have been added to the Method section: "Sensitivity analyses taken into account the differences in maternity leave policy in each country were also performed. These analyses were restricted to pregnant women who were not qualified for maternity leave (Supplementary Table 2) according to pregnancy week when the electronic questionnaire was completed".

**Table 2 (Supplementary Table 2 in the manucsript):** Descriptions of maternity leave in each participating country according to weeks prior to childbirth.<sup>4</sup>

Country	Maternity leave	Weeks before due date	Trimester
Croatia	28 days before the expected date of birth (45 days if there are complications resulting from the pregnancy)	6.4	3
Finland	50-30 days before the expected date of childbirth	7.1	3
France	Six weeks before	6	3
Italy	Two months before	8	3
Norway	3 weeks before	3	3
Poland	After childbirth	0	-
Russia	70 days before	10	3
Serbia	28 days before (first and second child)	4	3
Slovenia	28 days before	4	3
Sweden	60 days before	8.6	3
Switzerlan d	up to 196 francs, is paid for up to 98 days (14 weeks) after childbirth	0	-
United Kingdom	Maternity allowance: 15 weeks before	15	3
	Statutory maternity pay after childbirth		

In general, the results of these sensitivity analyses did not differ materially from the main analyses as presented in Table 3 below. However, the magnitude of the association between: i) NVP - both

medicated and non-medicated, and ii) sleeping problems - both medicated and non-medicated, with sick leave was greater than those observed in the main analysis. Also, the magnitude of the association between medication use for hypothyroidism and sick leave was lower than that observed in the main analysis. Given the overlapping confidence intervals of the main and sub-analysis estimates, as well as the small sample size in this sensitivity analysis (sleeping problems n=57 and hypothyroidism n=6), we feel that these sensitivity analysis results do not meaningfully change our main conclusions. These results may indicate that the differences in maternity leave policy did not have a remarkable influence our main analyses. The Results section has been amended with the following text: "The sensitivity analyses addressing the differences in maternity leave policy in each country showed that the magnitude of the association between having a medicated condition and sick leave did not differ materially from the main analyses (data not shown). These sensitivity analyses could not be done for hypothyroidism and sleeping problems due to small sample sizes".

**Table 3** Main analysis and sensitivity analysis of the independent variables and the association with sick leave during pregnancy, presented as crude (OR) and adjusted odds ratios (aOR) with the 95% confidence interval (95% CI).

Independent variables	Sick leave during pregnancy	
independent variables	Yes vs. no	
Chronic disorders	Main aOR (95% CI)	Sensitivity aOR (95% CI
Mood disorders		
No	Reference	Reference
Yes, non-medicated	2.05 (1.50-2.77)	2.03 (1.50-2.77)
Yes, medicated	3.14 (1.43-6.88)	3.07 (1.39-6.78)
Asthma		
No	Reference	Reference
Yes, non-medicated	2.22 (1.41-3.47)	1.96 (1.02-3.74)
Yes, medicated	1.32 (1.00-1.75)	1.51 (1.01-2.27)
Allergy		
No	Reference	Reference
Yes, non-medicated	1.51 (1.20-1.90)	1.53 (1.11-2.11)
Yes, medicated	1.49 (1.14-1.94)	1.27 (0.85-1.90)
Hypothyroidism		
No	Reference	Reference
Yes, non-medicated	2.68 (0.93-7.73)	1.45 (0.36-5.78)
Yes, medicated	1.41 (1.08-1.84)	1.57 (1.08-2.28)
Acute illnesses	aOR (95% CI)	

Nausea and vomiting			
No	Reference	Reference	
Yes, non-medicated	2.49 (1.58-3.93)	3.79 (1.81-7.92)	
Yes, medicated	4.52 (2.01-7.27)	7.03 (3.29-15.02)	
Pain			
No	Reference	Reference	
Pain, non-medicated	1.07 (0.85-1.36)	1.23 (0.86-1.77)	
Pain, medicated	1.38 (1.11-1.71)	1.49 (1.06-2.08)	
Sleeping problems (SP)			
No	Reference	Reference	
SP, non-medicated	3.09 (1.91-5.00)	4.59 (2.15-9.77)	
SP, medicated	5.42 (2.88-10.22)	8.22 (3.20-21.11)	

Missing data <5%. The multivariate models were adjusted for acute conditions (other than the one of interest), age, alcohol use in pregnancy, chronic conditions (other than the one of interest), education, employment, infertility treatment, marital status, maternal status, parity, planned pregnancy, and smoking in pregnancy.

### Major comment 6:

Lastly, although it is interesting to look at women with and without medication, I would focus the paper more around sick leave of women with or without certain health conditions. I believe that has more relevance for occupational and public health at the moment.

#### Reply 6:

The study was specifically designed to capture medication use according to different common illnesses and disorders in pregnancy. Given the widespread use of medications in pregnancy (80%)<sup>5</sup>, high rates of non-adherence<sup>1</sup>, and concerns about medication use<sup>6</sup> which could affect sick leave, we believe this perspective to be of major importance for occupational and public health. Nevertheless, our new analyses contrasting whether the chronic disorders were medicated or not medicated during pregnancy provides new insights into the effect of maternal diseases on sick leave. Please see Reply 1 for description of the amendments in the manuscript.

## Major comment 7

More discussion around how the results of this study can be used in improving work and/or health care of pregnant women, or reducing sick leave is also warranted in the paper.

### Reply 7:

As mentioned in Reply 6, our results may support the findings of previous studies that common pregnancy-related conditions, such as nausea and vomiting, are often neglected by healthcare personnel. It is surprising that medicated women for acute illnesses had a higher likelihood of being on sick leave compared with women with chronic disorders. These results may suggest that pregnant

The sensitivity analyses have been restricted to pregnant women who are not qualified for receiving maternity leave in each country as presented in Table 2 above.

Depression and/or anxiety.

<sup>\*\*\*</sup>Pain in the neck, back, or pelvic girdle, or headache.

women are not sufficiently treated for acute illnesses. If true, healthcare personnel should take this under advice. The manuscript has been amended as described in the end of Reply 1.

### Minor comments on typographical/grammatical errors 8:

- Line 57, page 4: "Furthermore, none of the previous studies.." this sentence can be deleted, since almost a duplicate of lines 10-11 on page 5.
- Multiple sick leave is used in several places, and in others extension of sick leave. Please use the last consistently.
- Page 14, line 45: .. than the one observed in the main analysis and **were** no longer significant. Delete "were".
- Page 18, line 4: .. could affect sick leave rates, distinguishing these sectors could have.. (delete "a" and "of".
- Page 18, line 23: shown instead of showed.
- Supplementary Figure 1: it is "The Netherlands", and not "The Netherland".

## Reply 8:

All typographical/grammatical errors have been addressed as advised.

#### Minor comment 9:

Page 7, lines 39-40: why did the authors focus on NVP, pain, and sleeping problems only? Some justification for this choice is needed.

#### Reply 9:

We focused on NVP, pain, and sleeping problems because these conditions were specifically stated as reasons for sick leave in pregnancy. We have added the following text into the Methods section: "For the acute pregnancy-related conditions we mainly focused on NVP, pain and sleeping problems because these conditions were specifically stated as reasons for sick leave".

# Minor comment 10:

Page 13 and 14: is discussing the differences between medications really relevant for the paper? It is a bit distracting, and makes a complicated paper even more complicated.

#### Replay 10:

We agree that those sections are less relevant and have now removed the concerned sections on page 13 and 14.

#### Minor comment 11:

Table 2: adding the % of medicated and non-medicated women in the column with Total would be helpful.

#### Reply 11:

Thank you, we have now done it.

## Minor comment 12:

Page 14, line 19: "Women from countries with "High" sick leave schemes had the..." Since this was only Norway, perhaps best rephrase as: "Women from Norway with a "High" sick leave scheme had the..."

#### Replay 12:

This sentence has been rephrased as advised.

### Minor comment 13:

Page 14, line 45: Medication use was no longer significant, but did the magnitude of the association change as well?

#### Reply 13:

The sensitivity analyses restricted to new mothers only showed that the associations between maternal medication use and sick leave in pregnancy did not differ much from the original analyses, with the exceptions of medication use for mood disorders and non-medication for hypothyroidism (57% increase and 100% decrease, respectively). The association between NVP and sleeping problems were found to be >35% and >25% lower, respectively, than in the original analyses. Given the small sample size in this sensitivity analysis (sleeping problems n=41 and hypothyroidism n=6), we believe that these sensitivity analysis results do not meaningfully change our main conclusions as described in Reply 5. The Results section has been amended as follows: "In the sensitivity analysis restricted to new mothers the magnitude of the associations between having a medicated condition and sick leave were generally similar to those of the main analysis (±20% change of the point estimates), with the exception of medicated mood disorders (+57% change) and non-medicated NVP (>35% lower) than in the original analyses (data not shown). These sensitivity analyses could not be done for hypothyroidism and sleeping problems due to small sample sizes". The following text has been added to the Discussion section: "The sensitivity analyses restricted to new mothers only showed that the magnitude of the association between medication use for NVP and sick leave was deflated and no longer significant. This may be explained by the fact that women with current conditions to a larger degree reported these conditions. NVP are especially known to occur in the beginning of the pregnancy".

#### Minor comment 14:

Page 18, line 50: again also describe if the magnitude of the associations changed, not only the significance, since the last is most influenced by sample size.

### Reply 14:

See Reply 13.

## Minor comment 15:

I believe more recent studies are available on sick leave in pregnancy that might be relevant for the discussion (e.g. Hansel ML, Thulstrup AM, Juhl M, et al. Predictors of sickness absence in pregnancy: a Danish cohort study. Scand. J Work Environ Health 2015;41(2):184-93)

#### Reply 15:

Thank you for this suggestion. As the suggested reference did not explore maternal illnesses in relation to sick leave in pregnancy, we find it challenging to compare the results to our study and hence include it in the discussion. However, we have now added the reference in the Introduction section.

# References:

- Lupattelli A, Spigset O, Nordeng H. Adherence to medication for chronic disorders during pregnancy: results from a multinational study. *Int J Clin Pharm* 2014;36:145-53.
- 2 Psychiatric Disorders in Pregnancy and the Postpartum: Principles and Treatment. Hendrick V, editor. Totawa, New Jersey: Humana Press; 2006.
- Heitmann K, Svendsen HC, Sporsheim IH, et al. Nausea in pregnancy: attitudes among pregnant women and general practitioners on treatment and pregnancy care. *Scand J Prim Health Care* 2016:1-8.
- 4 Social Security Administration. Soical Security Programs Throughout the World: Europe 2012 [Date accessed: June 2016 <a href="https://www.ssa.gov/policy/docs/progdesc/ssptw/2008-2009/europe/index.html">https://www.ssa.gov/policy/docs/progdesc/ssptw/2008-2009/europe/index.html</a>].
- 5 Lupattelli A, Spigset O, Twigg MJ, et al. Medication use in pregnancy: a cross-sectional, multinational web-based study. *BMJ Open* 2014;4.
- Petersen I, McCrea RL, Lupattelli A, et al. Women's perception of risks of adverse fetal pregnancy outcomes: a large-scale multinational survey. *BMJ Open* 2015;5:e007390.

# **VERSION 2 – REVIEW**

REVIEWER	Mireille van Poppel	
	Institute of Sport Science, University of Graz, Graz, Austria	
REVIEW RETURNED	02-Jun-2017	

GENERAL COMMENTS	I think the authors addressed previous comments adequately and i
	have not further comments.