PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Lumbopelvic pain, anxiety, physical activity and mode of conception: A prospective cohort study of pregnant women
AUTHORS	Lardon, Emeline; St-Laurent, Audrey; Babineau, Véronique; Descarreaux, M; Ruchat, Stephanie-May

VERSION 1 – REVIEW

REVIEWER	Daniela Aldabe University of Otago, New Zealand
REVIEW RETURNED	20-Mar-2018

GENERAL COMMENTS	Thank you for the opportunity to review this manuscript. This prospective cohort study investigated the relationship between mode of conception and PPGP, anxiety and physical activity levels. Findings are very interesting showing that mode of conception and anxiety is not related to PPGP throughout pregnancy. Overall the study is well presented, however, I have suggested some clarification that I believe will benefit the paper. **TITLE:** It does not seem the title correspond to the aims of the study. Was not PPGP the main factor of the study? The way title is presented seems that mode of conception is the main factor. **INTRODUCTION:** LINE 24 - 25: "PPGP represents the main cause of sick leave..." among women? pregnant women? Please, clarify. **MATERIAL & METHODS** LINE 9 – 20: Women were asked if they had PPGP in the last 7 days or presently each trimester. How this was done? Via e-mail? Face to face assessment? Please, clarify. In addition, what was your criteria to differentiate PGP from LBP? Because there is clearly a location overlap between LBP / PGP the authors should

	clarify that. If there were no differential criteria it is important to write about it as a limitation. LINE 29: Consider replacing “It is a…” for “The STAI is a…” LINE 9 – 15: “Women were allowed to remove the accelerometers in water activities.” I understand the accelerometer use has restrictions when using under immersion (according to manual it has to be used for 30 minutes only and immersion in one meter of water). However, this might create an underestimation of the physical activity levels. Pregnant populations are well-known by attending and being referred to aquatic activities, especially during the third trimester. I suggest the authors to explain this in the methods and add this as a limitation of the study. **RESULTS:** In general, all figures / labels were too small. I suggest replotting the graphs and make them twice as big. Also, do not use abbreviations in your figure legends. **DISCUSSION**: Page 11 LINE 53 – 56: Why it is very likely that OS and IUI generate less anxiety than IVF treatments? Authors should explain more about it as this is use as an explanation for no differences found between groups.

REVIEWER	Dragana Ceprnja Western Sydney University, Australia
REVIEW RETURNED	05-Apr-2018

GENERAL COMMENTS	In general, this cohort study reads well and adds to the body of knowledge of PPGP, in particular regarding maternal health related factors. Abstract - suggest rephrasing "we also examined the relationship between PPGP severity and anxiety" into an objective along the lines of " A further aim was to examine/explore the relationship between PPGP..." - in Results, suggest replacing the words "our outcomes" to "the outcome measures" Strengths and limitations - suggest rephrasing the first point from "... allowing to assess the evolution.." to "... allowing to determine/investigate the evolution..."

	Introduction - can you add reference for mention of quality of life? Suggest Olson & Nilsson-Wikmar reference for quality of life statement - provide some more rationale and information about physical activity in pregnancy (and PPGP). As it currently stands there is only one sentence in introduction about physical activity, yet it is the secondary objective. Discuss this more. - give some examples or brief summary of which factors are believed to be involved in PPGP development as opening sentences to paragraph Materials and Methods Study design - provide more detail about the setting (local and surrounding communities) - provide more detail about recruitment method Outcome measures and measurement tools - suggest rephrasing the sentence about using picture to localise pain to "lumbo-pelvic" region - to "pelvic girdle" region to clarify this study did not include women with lumbar spine pain - did you use physical examination tests to confirm diagnosis/classification of PPGP? Why or why not? - is there evidence for using the STAI in pregnant populations? Include this in rationale for using this tool. - any reasons why you preferred the PGQ to using other measures of physical activity in pregnancy, such as the Physical activity and pregnancy questionnaire or the Pregnancy Mobility Index? Statistical analysis - was there a priori sample size calculation performed? -how did you select the potential predictors of PPGP for logistic regression analyses? Provide rationale. Results - what are the reasons why 55 eligible pregnant women did not agree to participate? Include this information. - need to add the word "with" PPGP to line 14 (Among women presenting "with" PPGP...) and line 40 (Among women who presented "with" PPGP...) on page 9 Discussion - any discussion about the mean pain reported in your cohort (4/10) and how this compares to other studies, some of which have reported higher mean pain scores in the vicinity of 6/10 in studies of PPGP? - any discussion about the high incidence of reported PPGP in your cohort compared to prevalence data? Any local/national prevalence rates published? Limitations - line 19 this is second point raised not third, so change the word "Third, .." to "Second,..." Thus a pregnancy-specific anxiety tool may have been more appropriate to use? - do you have data about your local population and whether you would have expected half the women to have a university degree? or is your sample very different to local profile? - suggest changing the phrase "Moreover, our study clarifies the relationship..." to " Moreover, our study adds knowledge about the relationship ..." as accelerometer use has limitations with compliance and missing data (as you have previously pointed out).

REVIEWER	Arun Prasad Balasundaram University of Oslo, Norway
REVIEW RETURNED	10-Apr-2018

GENERAL COMMENTS	Reviewer comments I thank the Editor for providing me with an opportunity to review this paper. This study aimed to determine the evolution of pregnancy-related pelvic girdle pain (PPGP), anxiety, physical limitations and physical activity behaviours, and the respective associations between these variables. Major comments: 1. The manuscript has been written with a lot of ambiguity. It is confusing as to whether the objectives are in line with the methodology followed and the subsequent findings. 2. The use of continuous line numbers throughout the manuscript would have been more helpful, instead of having line numbers starting on each page. In this case, it is difficult in pointing to the text while making comments. 3. I think the title does not reflect the present aims of the study. The title states 'the relationship between mode of conception versus PPGP, anxiety and physical activity behaviours'. However, the mode of conception in this study has been used for making comparisons between the groups (spontaneous pregnancy vs fertility Tx induced pregnancy) rather than as an outcome. I suggest the authors re-word the title to reflect the current aims of their study. 4. Abstract: Lines 11-22, the objectives appear to be convoluted. Suggested to consider changing it to, all variables related to evolution as the first aim, and the focus on relationships as the second objective. While doing this, keep the context 'in women who conceived spontaneously (SP) or after fertility treatments (FT)' as a common one for both objectives, instead of having it only for the primary objective. 5. Introduction: Pg. 5, lines 7-20, the objectives could be re-stated to tease out the aims representing 'evolution' from 'associations' in order to improve clarity for the readers. Minor comments: 1. Suggest capitalizing 'a' before cohort in the title. 2. The citations in the reference list do not conform to the journal specifications. This is specifically true for the authors list and issue number. Please maintain consistency. 3. Abstract: a) Settings – I would be interested to see the exact health care settings (e.g.

	Hospitals, Clinics) in which the study was carried out. I would remove the method of recruitment (e.g. Posters) as stated here, this is not required. b) Pg. 3, lines 8-9. The authors state that clinical management of PPGP could minimise the physical limitations during pregnancy. This study did not test any interventions; therefore, this speculative statement should be removed. c) Pg. 3, lines 33-34, How does education limit the extrapolation of findings to wider populations? Please explain. 4. Pg. 4, line 42, The term 'prevalence' doesn't seem to be correct in this context. Change it to read as 'degree'. 5. Pg. 5, lines 3-4, The authors simply state without any justifications that additional studies are needed to confirm if higher levels of anxiety developed after fertility treatments result in PPGP. But this has already been established, and the authors themselves have referenced this in the previous sentences. Then why there is a need to further explore something that is already known. 6. Pg. 5, line 11, typo 'of', change to 'or'. 7. Pg. 5, Study design – I am aware that the study design has been mentioned in the abstract, however, this information must be re-written under the methods section. Where there any other inclusion and exclusion criteria apart from what has been provided? If so, please include further details. As I had commented earlier, it would be good to provide the type of setting in which the data were collected. 8. Pg. 6, line 16, typo 'had'. 9. Pg. 6, line 18, change the term 'evaluate' to read as 'rate'. I think 'rate' is an appropriate term, which you already have it in the subsequent sentences while referring to the VAS scale. 10. Pg. 6, line 22 - What picture was used? Was this pain drawings? More details required. 11. Pg. 6, line 42, What is PGQ? This is appearing for the first time in the manuscript, so needs expansion, abbreviation later is fine. 12. Pg. line 48, PGP is used here, elsewhere it is PPGP. Maintain consistency throughout the manuscript. 13. The physical activity (PA) levels using the accelerometer was assessed only for 7 days during each trimester. Given that each trimester, TR1 to TR3 lasted for more than a week, the data obtained and the results reported in relation to PA levels does not truly reflect the evolution of PA levels over the entire course of pregnancy.

	Therefore, this must be acknowledged under the limitations section. 14. Pg. 7, lines 45-47, Whether this is needed? Not sure, if the journal requires it. If not, please remove it. 15. Pg. 8, lines 16-17, now the authors are referring to predictors. No clue whatsoever leading from the introduction as to the aims to determine predictors of PPGP. 16. Whether the repeated measures data met the assumption of sphericity? If not, how was it corrected? More details are needed because often this assumption is violated in correlated data. 17. After closer examination of the results, it seems that a mixed-ANOVA was used but the authors report using repeated measures ANOVA. 18. A clear statement outlining the statistical procedures followed for each aim would help improve clarity. 19. In Figure 4c, the results reveal that there was a time vs group interaction (p=0.04). How did the authors explore further to understand this significant interaction? Have they carried out 'simple main effects'? If not, provide explanations because this is important when an interaction is significant. 20. Pg. 8, line 29, The information 'between Oct 2015 and May 2016' presented in results contradicts the one reported under the methods. 21. Pg. 9, line 5, was considered or being inactive, which one is true? 22. Pg. 9, line 18 and elsewhere, when reporting results following repeated measures ANOVA, it would be good to see the F values rather than just stating time effect. 23. Pg.10, lines 3-9, the results reported here are confusing. Investigated predictors of PPGP at TR3 but one of the candidate predictors was PPGP at TR1. This way of testing appears to be related, thus creating a potential for circular logic, which may lead to spurious findings. I am also confused as to why logistic regressions were used. The effect of anxiety levels, physical limitations and physical activity on PPGP between the SP and FT groups were already tested using an ANOVA model. Then why again to test using a different statistical (logistic regression) approach with the inclusion of some additional variables such as BMI, parity and so forth. Please explain. 24. If the use of logistic regressions is justified with valid reasons, then a table with detailed results such as coefficient values, standard errors and CIs' should be provided for interpretation of the study findings. 25. Pg. 12, line 50, there is a mention of univariate approach here. This should have been

	under the statistical analysis section. 26. Pg. 13, line 23, the authors acknowledge that physical activity variable had missing data. How was it resolved? – which method was used for handling missing data before subjecting it to statistical analysis?

REVIEWER	Jan Mens Erasmus University Rotterdam, the Netherlands
REVIEW RETURNED	11-Apr-2018

GENERAL COMMENTS	1. I am very happy with this study because of the following. The present study describes the relation between mode of conception and PGP. In a previous study (Kristiansson, 1998) found that PGP was more frequent in women who conceived by means of IVF. However in that study many women carried multiple pregnancies. They wrote: “When the influence of serum relaxin concentration on back pain prevalence was taken into account, women carrying multiple pregnancies had no more pain than women carrying singletons, and IVF pregnant women had no more pain than spontaneously pregnant women.” However since relaxin levels are higher after IVF, and the number of fetuses is higher after IVF it is difficult to indicate what is cause of higher rates of PGP after IVF. Kristiansson et al concluded that relaxine causes PGP. As a consequence IVF and twin pregnancies have more chance to develop PGP because relaxin is higher in twin pregnancies and after IVF pregnancies. However they disregard another cause-effect relation: twin pregnancies cause more frequent PGP because the mechanical load is higher. As a consequence IVF and higher relaxin levels correlate with PGP. The present study with singleton-pregnancies shows that it is not the IVF or the relaxin that caused the high rates of PGP in the study of Kristiansson. Perhaps you could add some lines about this in the discussion. 2. You added 13 figures. I believe that you could reduce the number. Perhaps they are all superfluous.

REVIEWER	Line Riis Jølving, PhD Odense Universitetshospital, Center for Clinical Epidemiology
REVIEW RETURNED	04-Jun-2018

GENERAL COMMENTS	A well written manuscript including a clear objective and methodology. I have one major concern regarding the statistical power related to the following two issues: 1) The size of the study popuation of only 26 FT women which only the 7 women undervent IVF treatment that is indicated to be the one single factor in the fertility tretment that is most likely to be related to the outcomes of interest. The authors adress this limitation, however one might argue that the study hypothesis can not be fully falsified by this studypopulation (though I fully acknowledge the difficulties in recruitment of the pregnant women).

VERSION 1 – AUTHOR RESPONSE

Reviewers' comments:

Reviewer #1:

Title

Comment 1*: It does not seem the title correspond to the aims of the study. Was not PPGP the main factor of the study? The way title is presented seems that mode of conception is the main factor.*

Response 1: As recommended by the reviewer, we modified the title of the revised manuscript to better reflect the aims of the study. The new title is:

Lumbopelvic pain, anxiety, physical activity and mode of conception: a prospective cohort study of pregnant women.

We replaced “pelvic girdle pain” by “lumbopelvic pain” in the revised title to address comment 3 of the reviewer.

Introduction

Comment 2*: LINE 24 - 25: "PPGP represents the main cause of sick leave..." among women? pregnant women? Please, clarify.*

Response 2: To address comment 4 of the reviewer #2, we reworded a sentence of the introduction. *"PPGP represents the main cause of sick leave..."* has been reworded. Please see below our response to comment 4 - reviewer #2.

Material and methods

Comment 3*: LINE 9 – 20: Women were asked if they had PPGP in the last 7 days or presently each trimester. How this was done? Via e-mail? Face to face assessment? Please, clarify. In addition, what was your criteria to differentiate PGP from LBP? Because there is clearly a location overlap between LBP / PGP the authors should clarify that. If there were no differential criteria it is important to write about it as a limitation.*

Response 3: We thank the reviewer for this thoughtful comment. We did not differentiate PGP from LBP and the reviewer is right, there is a location overlap between LBP/PGP. We therefore used the term “lumbopelvic pain (LPP)” instead of PGP in the revised manuscript. We also reworded the first part of the introduction to clarify the difference between LBP and PGP and why the term LPP. The first part of the introduction was reworded as follows:

Low back pain (LBP) is defined as pain localized below the ribs, but above the gluteal folds, with or without radiation down the legs [2], whereas pelvic girdle pain (PGP) has been defined as pain “experienced between the posterior iliac crest and the gluteal fold, particularly in the vicinity of the sacroiliac joints. The pain may radiate in the posterior thigh and can also occur in conjunction with/or separately in the symphysis” [1]. The term lumbopelvic pain (LPP) is used when no distinction is made between PGP and LBP [3].

We clarified how LPP was assessed in the revised manuscript. We added the following information on page 6:

In each trimester, a member of the research team asked the women if they have had pregnancy-related LPP over the last 7 days or if they were having LPP presently using the illustration provided in the French version of the Pelvic Girdle Questionnaire (PGQ) [19].

Comment 4*: LINE 29: Consider replacing “It is a…” for “The STAI is a…”*

Response 4: The suggested modification was done in the revised manuscript.

Comment 5*: LINE 9 – 15: "Women were allowed to remove the accelerometers in water activities." I understand the accelerometer use has restrictions when using under immersion (according to manual it has to be used for 30 minutes only and immersion in one meter of water). However, this might create an underestimation of the physical activity levels. Pregnant populations are well-known by attending and being referred to aquatic activities, especially during the third trimester. I suggest the authors to explain this in the methods and add this as a limitation of the study.*

Response 5: We thank the reviewer for this thoughtful comment. We are aware that non-waterproof accelerometer underestimates several types of physical activity, such as water activities. It is therefore possible that we underestimated the level of physical activity for some participants who removed the accelerometer to do water activities. In our data set, a total of 8 (13.5%), 8 (13.5%) and 9 (15%) women removed the accelerometer to do water activities (aqua gym, swimming or bathing) during TR1, TR2 and TR3, respectively. The accelerometer was removed between 1 and 5 times during the evaluation period, and for 10 to 225 minutes. We may therefore have underestimated physical activity levels for these women. We added the following information in the revised manuscript:

Page 9 (result section): *In our study, a total of 8 (13.5%), 8 (13.5%) and 9 (15%) women removed the accelerometer to do water activities (aqua gym, swimming or bathing) during TR1, TR2 and TR3, respectively. The accelerometer was removed between 1 and 5 times during the evaluation period, and for 10 to 225 minutes.*

Page 13 (discussion section): *Third, although accelerometers provide a valid and objective measure of physical activity levels, non-waterproof accelerometers underestimate several types of physical activity, such as water activities. In our data set, several women removed the accelerometer to do water activities (aqua gym, swimming or bathing) during TR1, TR2 and TR3, suggesting that we possibly underestimated the level of physical activity of these women.*

Results

Comment 6*: In general, all figures / labels were too small. I suggest replotting the graphs and make them twice as big. Also, do not use abbreviations in your figure legends.*

Response 6: We replotted the graphs and made them bigger. Moreover, we remove the use abbreviation in the figure legends. In figures where we used abbreviation (due to space limitation), we added a footnote to define the abbreviation.

Discussion

Comment 7*: Page 11 LINE 53 – 56: Why it is very likely that OS and IUI generate less anxiety than IVF treatments? Authors should explain more about it as this is use as an explanation for no differences found between groups.*

Response 7: We thank the reviewer for this comment. We added the following information on page 12 in the revised manuscript:

Because the medical surveillance is more frequent and the procedure more invasive in the context of IVF, it is likely that IVF generates more anxiety than OS and IUI. This might partially explain why we found no differences in anxiety levels in our sample.

Reviewer #2:

Abstract

Comment 1*: Suggest rephrasing "we also examined the relationship between PPGP severity and anxiety" into an objective along the lines of "A further aim was to examine/explore the relationship between PPGP..."*

Response 1: As suggested by the reviewer, we modified the wording of the sentence in the revised manuscript.

Comment 2: *In Results, suggest replacing the words "our outcomes" to "the outcome measures"*

Response 2: As suggested by the reviewer, we modified the wording in the revised manuscript.

Strengths and limitations

Comment 3*: Suggest rephrasing the first point from "... allowing to assess the evolution..." to "... allowing to determine/investigate the evolution..."*

Response 3: As suggested by the reviewer, we modified the wording in the revised manuscript.

Introduction

Comment 4*: Can you add reference for mention of quality of life? Suggest Olson & Nilsson-Wikmar reference for quality of life statement.*
Response 4: We added the reference from Olson & Nilsson-Wikmar in the revised manuscript to support the sentence about quality of life. We also slightly modified a sentence on page 4. The modified sentence reads now as:

Pregnancy-related LPP is a debilitating condition that is known to affect women's quality of life [7], with repercussions such as disruption of sleep, increased psychological stress, social and sexual life and work capacity [4 7-10].

Comment 5*: Provide some more rationale and information about physical activity in pregnancy (and PPGP). As it currently stands there is only one sentence in introduction about physical activity, yet it is the secondary objective. Discuss this more.*

Response 5: We provided some more rationale and information about physical activity in pregnancy and PPGP in the revised manuscript. We added the following information on page 4:

Pregnant women experiencing LPP are also known to be less physically active during pregnancy [11]. Prenatal physical activity is an important component of a healthy pregnancy [12] and all women without contraindication to exercise are encouraged to be regularly active throughout pregnancy to benefit from it [13 14]. On the other hand, pregnancy-related LPP can contribute to maternal physical inactivity and its associated maternal, fetal and neonatal complications[12].

Comment 6*: Give some examples or brief summary of which factors are believed to be involved in PPGP development as opening sentences to paragraph.*

Response 6: We provided some examples of factors that are believed to be involved in PPGP development in the revised manuscript. The following information was added on page 4:

Several factors are believed to be involved in pregnancy-related LPP development, such as degenerative metabolic, genetic, hormonal, and biomechanical factors/non-optimal joint stability [1 6].

Material and methods

Study design

Comment 7 and 8: *Provide more detail about the setting (local and surrounding communities). Provide more detail about recruitment method.*

Response 7 and 8: We provided more detail about the setting in the revised manuscript. We added the following information on page 6:

Women who achieved a spontaneous pregnancy (SP group) and women who achieved pregnancy following fertility treatments (FT group) were recruited through physicians' and a clinic coordinator's referrals, posters and newspaper advertisements in the local and surrounding communities (hospital, maternity care clinic, prenatal centers, sports centers, local university).

Reviewer #3 suggested removing detail about recruitment method (see comment 8). We therefore did not provide more detail about recruitment method.

Outcome measures and measurement tools

Comment 9*: Suggest rephrasing the sentence about using picture to localise pain to "lumbo-pelvic" region - to "pelvic girdle" region to clarify this study did not include women with lumbar spine pain.*

Response 9: To address comment 3 of reviewer #1, we replaced "pelvic girdle pain" by "lumbopelvic pain" in the revised manuscript. Keeping the mention of the *"lumbopelvic" region* in the revised manuscript is now appropriate.

Comment 10*: Did you use physical examination tests to confirm diagnosis/classification of PPGP? Why or why not?*

Response 10: For feasibility reasons, we did not use physical examination tests to confirm diagnosis/classification of pregnancy-related LPP. Participation to the project required an important time commitment and adding one physical examination at each trimester would have required additional time commitment from the women, with the risk of decreasing our recruitment rate.

Comment 11*: Is there evidence for using the STAI in pregnant populations? Include this in rationale for using this tool.*

Response 11: Yes, the STAI has been frequently used in pregnant populations. We added the following information on page 7 in the revised manuscript to provide rationale for using this tool:

The STAI has been widely used in research with pregnant women and it does reflect the anxiety-related experiences of pregnant women. Its use with pregnant women is therefore appropriate [23].

Comment 12*: Any reasons why you preferred the PGQ to using other measures of physical activity in pregnancy, such as the Physical activity and pregnancy questionnaire or the Pregnancy Mobility Index?*

Response 12: As mentioned in the method section, we used the PGQ to assess activity limitations and symptoms associated with pregnancy-related LPP and not to assess physical activity levels. We used the accelerometer to assess physical activity levels. We chose to use the French version of the PGQ because it is the only condition-specific tool for assessing activity limitations and symptoms associated with LPP in pregnant women.

Statistical analysis

Comment 13*: Was there a priori sample size calculation performed?*

Response 13: No *a priori* sample size calculation was performed.
Comment 14*: How did you select the potential predictors of PPGP for logistic regression analyses? Provide rationale.*

Response 14: Based on the comments of two reviewers about the exploratory logistic regression analyses and the amount of results and figures we are reporting and based on extensive discussion with the authors of the manuscript, we have decided to remove the exploratory regression analysis from the revise manuscript.

Results

Comment 15*: What are the reasons why 55 eligible pregnant women did not agree to participate? Include this information.*

Response 15: We thank the reviewer for this comment. The reasons why 55 eligible pregnant women did not agree to participate to the study were because of lack of interest or lack of time. We added this information on page 9 in the revised manuscript.

Comment 16*: Need to add the word "with" PPGP to line 14 (Among women presenting "with" PPGP...) and line 40 (Among women who presented "with" PPGP...) on page 9.*

Response 16: We made the correction in the revised manuscript.

Discussion

Comment 17*: Any discussion about the mean pain reported in your cohort (4/10) and how this compares to other studies, some of which have reported higher mean pain scores in the vicinity of 6/10 in studies of PPGP?*

Response 17: We thank the reviewer for this comment. Other studies have reported mean/median pain scores for both LBP and PGP within the range of values obtained in our studies. Kovacs et al. (Spine (Phila Pa 1976) 2012;37(17):1516-33) followed 1,158 women during four weeks and reported a median pain score of 5 for LBP and median score of 4 for PGP. Another study by Wang et al. (Obstet Gynecol. 2004;104(1):65-70) showed an average pain (LBP) of 45.6/100 in a sample of more than a 1,000 women from which 68.6% reported back pain during pregnancy. We added the following information on page 11 of the revised manuscript:

As expected, the prevalence and severity of LPP increased over the course of pregnancy and were of similar magnitude than that reported in previous studies [10 18].

Comment 18*: Any discussion about the high incidence of reported PPGP in your cohort compared to prevalence data? Any local/national prevalence rates published?*

Response 18: As mentioned above (please see response to comment 3 - reviewer 1), we reworded the first part of the introduction section. Prevalence data have been adjusted for the lumbopelvic area. We modified the prevalence data on page 4 in the revised manuscript:
More than 50% of women experience pain in the lumbopelvic area during pregnancy [1]. Low back pain (LBP) is defined as pain localized below the ribs, but above the gluteal folds, with or without radiation down the legs [2], whereas pelvic girdle pain (PGP) is defined as pain "experienced between the posterior iliac crest and the gluteal fold, particularly in the vicinity of the sacroiliac joints. The pain may radiate in the posterior thigh and can also occur in conjunction with/or separately in the symphysis" [1]. The term lumbopelvic pain (LPP) is used when no distinction is made between PGP and LBP [3]. Thus the wide range in the reported prevalence of LPP in the literature (45–73%) [4 5] has been attributed to the different criteria used to classify types and severity of pain, and different periods during pregnancy LPP was assessed.

According to these prevalence data, we consider that we are not reporting high incidence of LPP in our cohort.

Limitations

Comment 19*: LINE 19: this is second point raised not third, so change the word "Third, .." to "Second,..." Thus a pregnancy-specific anxiety tool may have been more appropriate to use?*

Response 19: We thank the reviewer for this comment. No, a pregnancy-specific anxiety tool may not have been more appropriate to use since the STAI does reflect the anxiety-related experiences of pregnant women. This point has been removed from the discussion and limitations of the study.

Comment 20*: Do you have data about your local population and whether you would have expected half the women to have a university degree? or is your sample very different to local profile?*

Response 20: We did not expect half of the women to have a university degree but it turns out that in our sample, half of the women have a university degree. Based on statistics on the highest level of education attained in our local population, 22.5% of adults had a university degree in 2016 (Institut de la statistique Québec - Distribution of the population aged 25 to 64 by highest level of education attained, Mauricie and all of Québec, 2012-2016). Consequently, in terms of education levels, our sample does not reflect our local population. This was discussed as a limitation in the submitted manuscript (see page 13). We added a piece of information to clarify the discussed limitation:

Second, more than half of the women we recruited had a university degree, which is more than in our local population (22.5%) [41].

***Comment 21**: Suggest changing the phrase "Moreover, our study clarifies the relationship..." to " Moreover, our study adds knowledge about the relationship ..." as accelerometer use has limitations with compliance and missing data (as you have previously pointed out).*

Response 21: As suggested by the reviewer, we modified the sentence in the revised manuscript.

Reviewer #3:

Major comments:

***Comment 1**: The manuscript has been written with a lot of ambiguity. It is confusing as to whether the objectives are in line with the methodology followed and the subsequent findings.*
Response 1: We hope that the changes that were made in the revised version of the manuscript to address the comments of the five reviewers clarified the elements that the reviewer found ambiguous.

***Comment 2**: The use of continuous line numbers throughout the manuscript would have been more helpful, instead of having line numbers starting on each page. In this case, it is difficult in pointing to the text while making comments.*

Response 2: The use of line numbers starting on each page was automatically done during the on-line submission process.

***Comment 3**: I think the title does not reflect the present aims of the study. The title states 'the relationship between mode of conception versus PPGP, anxiety and physical activity behaviours'. However, the mode of conception in this study has been used for making comparisons between the groups (spontaneous pregnancy vs fertility Tx induced pregnancy) rather than as an outcome. I suggest the authors re-word the title to reflect the current aims of their study.*

Response 3: We modified the title of the manuscript to better reflect the aims of the study (please see response to comment 1 - reviewer #1).

***Comment 4**: Abstract: Lines 11-22, the objectives appear to be convoluted. Suggested to consider changing it to, all variables related to evolution as the first aim, and the focus on relationships as the second objective. While doing this, keep the context 'in women who conceived spontaneously (SP) or after fertility treatments (FT)' as a common one for both objectives, instead of having it only for the primary objective.*

Response 4: Our primary and secondary objectives are based on our primary outcomes (i.e. pregnancy-related LPP and anxiety) and secondary outcomes (physical activity behaviours) and are not based on how the variables would change over the course of pregnancy or on how they would relate to each other. Therefore, we cannot change the objectives as suggested by the reviewer.

***Comment 5**: Introduction: Pg. 5, lines 7-20, the objectives could be re-stated to tease out the aims representing 'evolution' from 'associations' in order to improve clarity for the readers.*

Response 5: As responded to the previous comment, we cannot re-state the objectives as suggested (please see our response to comment 4).

Minor comments:

Comment 6*: Suggest capitalizing 'a' before cohort in the title.*

Response 6: As suggested by the reviewer, we capitalized the "a" in the title.

Comment 7*: The citations in the reference list do not conform to the journal specifications. This is specifically true for the authors list and issue number. Please maintain consistency.*

Response 7: In the revised manuscript, we carefully verified that the reference list does conform to the journal specifications.

Abstract:

Comment 8*: Settings – I would be interested to see the exact health care settings (e.g. Hospitals, Clinics) in which the study was carried out. I would remove the method of recruitment (e.g. Posters) as stated here, this is not required.*

Response 8: As clarified above (please see response 7 and 8 to reviewer #2), we provided more detail about the setting in which the study was carried out.

Comment 9*: Pg. 3, lines 8-9. The authors state that clinical management of PPGP could minimise the physical limitations during pregnancy. This study did not test any interventions; therefore, this speculative statement should be removed.*

Response 9: We removed the last sentence of the abstract's conclusion, as recommended by the reviewer.

Comment 10*: Pg. 3, lines 33-34, How does education limit the extrapolation of findings to wider populations? Please explain.*

Response 10: The fact that our population was more educated than the local population prevents us to generalize the relationships, or the absence of relationships, we found in our study. Specifically, the relationship between pregnancy-related LPP and anxiety or physical activity behaviours might be influenced by education level of the women (e.g. more educated women may be aware that LPP is common during pregnancy and will not affect (or will affect to a lesser degree) their anxiety level.

Comment 11*: Pg. 4, line 42, The term 'prevalence' doesn't seem to be correct in this context. Change it to read as 'degree'.*

Response 11: In this sentence, we are talking about the results of the pelvic pain provocation tests that can be positive or negative. In this context, it is inadequate to use the term "degree". The term "prevalence" might not be the most appropriate and we therefore changed it to "frequency" of positive results on pelvic pain provocation tests.

Comment 12*: Pg. 5, lines 3-4, The authors simply state without any justifications that additional studies are needed to confirm if higher levels of anxiety developed after fertility treatments result in PPGP. But this has already been established, and the authors themselves have referenced this in the previous sentences. Then why there is a need to further explore something that is already known.*

Response 12: We thank the reviewer for his comment. One study reported that women who conceived following fertility treatments had greater pregnancy-specific anxiety than those who conceived naturally. Another study reported that anxiety was associated with LBP. However, no studies examined pregnancy-related LPP among women who achieve a pregnancy naturally or after fertility treatment, and whether anxiety is a contributing factor to the development of LPP. On page 5 of the revised manuscript, we reworded the sentence to make this research gap clearer.

***Comment 13**: Pg. 5, line 11, typo 'of', change to 'or'.*

Response 13: The typo has been corrected in the revised manuscript.

***Comment 14**: Pg. 5, Study design – I am aware that the study design has been mentioned in the abstract, however, this information must be re-written under the methods section. Where there any other inclusion and exclusion criteria apart from what has been provided? If so, please include further details. As I had commented earlier, it would be good to provide the type of setting in which the data were collected.*

Response 14: There was no other inclusion and exclusion criterion apart from what we provided in the submitted manuscript. We re-wrote the study design under the methods section. In the abstract of the revised manuscript, we provided the type of setting in which the data were collected (please see response 7 and 8 to reviewer #2).

***Comment 15**: Pg. 6, line 16, typo 'had'.*

Response 15: The typo has been corrected in the revised manuscript.

***Comment 16**: Pg. 6, line 18, change the term 'evaluate' to read as 'rate'. I think 'rate' is an appropriate term, which you already have it in the subsequent sentences while referring to the VAS scale.*

Response 16: We used the term 'rate' instead as 'evaluate' in the revised manuscript.

***Comment 17**: Pg. 6, line 22 - What picture was used? Was this pain drawings? More details required.*

Response 17: As clarified above (please see response to comment 3 - reviewer #1), we provided more details about the illustration we used in the revised manuscript.

***Comment 18:** Pg. 6, line 42, What is PGQ? This is appearing for the first time in the manuscript, so needs expansion, abbreviation later is fine.*

Response 18: Thank you for having pointed out this mistake. We made the correction and wrote in full "PGQ" the first time it appears (on page 6).

***Comment 19**: Pg. line 48, PGP is used here, elsewhere it is PPGP. Maintain consistency throughout the manuscript.*
Response 19: We made the change in the revised manuscript.

***Comment 20**: The physical activity (PA) levels using the accelerometer was assessed only for 7 days during each trimester. Given that each trimester, TR1 to TR3 lasted for more than a week, the data obtained and the results reported in relation to PA levels does not truly reflect the evolution of PA levels over the entire course of pregnancy. Therefore, this must be acknowledged under the limitations section.*

Response 20: We thank the reviewer for this thoughtful comment. We agree that this is a limitation to discuss in the manuscript. We added the following information on page 13 in the revised manuscript:

Finally, physical activity levels were assessed only for a seven-day period during each trimester of pregnancy. Given that each trimester lasts for more than a week, the data obtained and the results reported in relation to physical activity levels don't truly reflect the evolution of physical activity levels over each trimester and over the entire course of pregnancy. Nevertheless, the majority of the women stated in the daily diary that their physical activity behavior over the seven-day period of evaluation reflected their habitual behaviors.

***Comment 21:** Pg. 7, lines 45-47, Whether this is needed? Not sure, if the journal requires it. If not, please remove it.*

Response 21: Yes, the journal requires this information.

Comment 22: *Pg. 8, lines 16-17, now the authors are referring to predictors. No clue whatsoever leading from the introduction as to the aims to determine predictors of PPGP.*

Response 22: Please see response to comment 14 – reviewer 2. We have decided to remove the exploratory regression analysis from the revise manuscript.

Comment 23: *Whether the repeated measures data met the assumption of sphericity? If not, how was it corrected? More details are needed because often this assumption is violated in correlated data.*

Response 23: We thank the reviewer for this comment. The assumption of sphericity was tested using Mauchly's Test of Sphericity. All variables met the assumption of sphericity with the exception of "daily steps" (Mauchly's Test p=0.0445) which was analyzed following a Geisser Greenhouse correction. As reported in the original version of the manuscript, a significant time effect was present for daily steps following the Geisser Greenhouse correction (time effect: F=16.03, p<0.0001). We clarified this on page 8 of the revised manuscript:

The assumption of sphericity was tested using Mauchly's Test of Sphericity. Variables that did not meet the sphericity assumption were analyzed following a Geisser Greenhouse correction. When

Comment 24: *After closer examination of the results, it seems that a mixed-ANOVA was used but the authors report using repeated measures ANOVA.*

Response 24: The reviewer is correct, we used the MIXED procedure of SAS (SAS Institute, Cary, NC, version 9.4) to test the effect of time (trimesters), group (SP and FT women) and interactive effect on the outcome measures. We clarified this on page 8 of the revised manuscript:

The MIXED procedure of SAS was used to test the effect of time (trimesters), group (SP and FT women) and potential interaction effects on the outcome measures (i.e. the severity of pregnancy-related LPP and anxiety levels [objective 1], and physical activity behaviors [objective 2]).

Comment 25: *A clear statement outlining the statistical procedures followed for each aim would help improve clarity.*

Response 25: As suggested by the reviewer, we clarified in the revised manuscript which statistical procedure was used for each aim of the study.

Comment 26: *In Figure 4c, the results reveal that there was a time vs group interaction (p=0.04). How did the authors explore further to understand this significant interaction? Have they carried out 'simple main effects'? If not, provide explanations because this is important when an interaction is significant.*

Response 26: We thank the reviewer for this comment. To clarify how we further explored significant main and interactive effect, we added on page 8 of the revised manuscript the following sentence:

When a significant effect of time, group or interaction effect was found, post-hoc analyses were conducted using the Tukey test.

Comment 27: *Pg. 8, line 29, The information 'between Oct 2015 and May 2016' presented in results contradicts the one reported under the methods.*

Response 27: Thank you for having pointed out this mistake. We made the correction in the revised manuscript.

Comment 28: *Pg. 9, line 5, was considered or being inactive, which one is true?*

Response 28: Based on the recommendations we are referring to, our sample was considered inactive, which means that they were inactive. Both wording have the same meaning.

Comment 29: *Pg. 9, line 18 and elsewhere, when reporting results following repeated measures ANOVA, it would be good to see the F values rather than just stating time effect.*

Response 29: As suggested by the reviewer, we added F values to the results obtained using repeated measures ANOVA in the revised manuscript.

Comment 30: *Pg.10, lines 3-9, the results reported here are confusing. Investigated predictors of PPGP at TR3 but one of the candidate predictors was PPGP at TR1. This way of testing appears to be related, thus creating a potential for circular logic, which may lead to spurious findings. I am also confused as to why logistic regressions were used. The effect of anxiety levels, physical limitations and physical activity on PPGP between the SP and FT groups were already tested using an ANOVA model. Then why again to test using a different statistical (logistic regression) approach with the inclusion of some additional variables such as BMI, parity and so forth. Please explain.*

Response 30: Please see response to comment 14 – reviewer 2. We have decided to remove the exploratory regression analysis from the revise manuscript.

Comment 31: *If the use of logistic regressions is justified with valid reasons, then a table with detailed results such as coefficient values, standard errors and CIs' should be provided for interpretation of the study findings.*

Response 31: Please see response to comment 14 – reviewer 2. We have decided to remove the exploratory regression analysis from the revise manuscript.

Comment 32: *Pg. 12, line 50, there is a mention of univariate approach here. This should have been under the statistical analysis section.*

Response 32: Please see response to comment 14 – reviewer 2. We have decided to remove the exploratory regression analysis from the revise manuscript.

Comment 33: *Pg. 13, line 23, the authors acknowledge that physical activity variable had missing data. How was it resolved? – which method was used for handling missing data before subjecting it to statistical analysis?*

Response 33*:* We thank the reviewer for this comment. Our data were missing completely at random, which means that the missing values have nothing to do with their hypothetical value and with the values of other variables. For example, LPP severity during TR1, TR2 and TR3 was similar between women for whom we have physical activity data and for whom we don't have physical activity data. In such a case, it is judged safe to remove the data with missing values and this is what we did.

Reviewer #4:

Comment 1*: I am very happy with this study because of the following.*

The present study describes the relation between mode of conception and PGP. In a previous study (Kristiansson, 1998) found that PGP was more frequent in women who conceived by means of IVF. However in that study many women carried multiple pregnancies. They wrote: "When the influence of serum relaxin concentration on back pain prevalence was taken into account, women carrying multiple pregnancies had no more pain than women carrying singletons, and IVF pregnant women had no more pain than spontaneously pregnant women."
However since relaxin levels are higher after IVF, and the number of fetuses is higher after IVF it is difficult to indicate what is cause of higher rates of PGP after IVF.
Kristiansson et al concluded that relaxine causes PGP. As a consequence IVF and twin pregnancies have more chance to develop PGP because relaxin is higher in twin pregnancies and after IVF pregnancies. However they disregard another cause-effect relation: twin pregnancies cause more frequent PGP because the mechanical load is higher. As a consequence IVF and higher relaxin levels correlate with PGP.
The present study with singleton-pregnancies shows that it is not the IVF or the relaxin that caused the high rates of PGP in the study of Kristiansson.
Perhaps you could add some lines about this in the discussion.

Response 1: We thank the reviewer for this valuable comment. As recommended, we added some lines about the studies by Kristiansson et al. in the discussion of the revised manuscript. The following information was added on page 11:

Importantly, many IVF women carried multiple pregnancies in that study. Given that relaxin levels are higher after IVF [16] and that the number of fetuses is higher after IVF, and given that the mechanical load is higher in twin pregnancies, it is difficult to establish what causes higher rates of PPGP after IVF in this previous study.

***Comment 2**: You added 13 figures. I believe that you could reduce the number. Perhaps they are all superfluous.*

Response 2: We believe that figures provide a visual summary of the results and are helpful to the reader. We are therefore in favor of keeping the figures in the manuscript, unless the editorial office asks us to remove them (or some of them).

Reviewer #5:

***Comment 1**: A well written manuscript including a clear objective and methodology. I have one major concern regarding the statistical power related to the following two issues: 1) The size of the study population of only 26 FT women which only the 7 women underwent IVF treatment that is indicated to be the one single factor in the fertility treatment that is most likely to be related to the outcomes of interest. The authors address this limitation, however one might argue that the study hypothesis cannot be fully falsified by this study population (though I fully acknowledge the difficulties in recruitment of the pregnant women).*

Response 1: We thank the reviewer for this comment. We agree that our sample size is small and that given the low number of women who achieved a pregnancy following IVF, our hypotheses cannot be fully tested. However, our study adds knowledge about the relationship between PPGP severity and physical activity behaviors. We added the following sentence on page 13 in the revised manuscript to better acknowledge this limitation:

The low number of women who achieved a pregnancy following IVF prevented us to fully test our hypotheses and further larger studies are needed to better understand whether IVF contribute to pregnancy-related.

FORMATTING AMENDMENTS FROM EDITORIAL OFFICE:

***Comment 1**: Figures 3-6 (Sub figures uploaded separately)*
Please combine your uploaded sub figures into one to have a single file figure and make sure that they have a resolution of at least 300 dpi. Figures in PDF, DOCUMENT, EXCEL and POWER POINT format are not acceptable. Note: If you can't convert your figure into one, kindly renumber the figure legends into Figure 1, Figure 2, etc.

Response 1: We will make sure to follow the Figure formatting requested by the editorial office. We were not able to convert the sub figures into one so we renumber the figure legends into Figure 1, Figure 2, etc.

VERSION 2 – REVIEW

REVIEWER	Daniela Aldabe University of Otago
REVIEW RETURNED	24-Jul-2018

GENERAL COMMENTS	Page 7 line 4 to 6 - Please consider rewriting it in a simpler and concise way.

	Page 7 line 22 - Replace characters for full description. Page 9 line 6 - "... the study was presented by physicians or to 117..." does not make sense. Please correct it.

REVIEWER	Dragana Ceprnja Western Sydney University, Australia
REVIEW RETURNED	17-Jul-2018

GENERAL COMMENTS	The authors have addressed my previous comments. The resulting manuscript adds knowledge about lumbo-pelvic pain and maternal health factors. Just two comments from me: Abstract - Setting Can you add information about the location of study? eg. City, Country Also add this information to the Materials and Methods section. Introduction Suggest psychosocial factors may also be involved in the development of lumbo-pelvic pain.

REVIEWER	Line Riis Jølving Odense University Hospital, Odense Denmark
REVIEW RETURNED	20-Aug-2018

GENERAL COMMENTS	The abstract and the body text could need a proof reading in terms of the use of space between the words.

VERSION 2 – AUTHOR RESPONSE

Reviewers' comments:

Reviewer #1:

Comment 1: Page 7 line 4 to 6 - Please consider rewriting it in a simpler and concise way.

Response 1: In the revised version of the manuscript, the sentence has been reworded as:

Each scale comprises 20 items rated with a 4-level Likert scale.

Comment 2: Page 7 line 22 - Replace characters for full description.

Response 2: In the revised version of the manuscript, we replaced characters for full description.

Comment 3: Page 9 line 6 - "... the study was presented by physicians or to 117..." does not make sense. Please correct it.

Response 3: In the revised version of the manuscript, we made the correction; we removed the “or”.

Reviewer #2:

Abstract - Setting

Comment 1*: Can you add information about the location of study? eg. City, Country. Also add this information to the Materials and Methods section.*

Response 1: As requested by the reviewer, we added in the abstract and Materials and Methods section of the revised version of the manuscript the name of the city and country where the study was conducted.

Introduction

Comment 2*: Suggest psychosocial factors may also be involved in the development of lumbo-pelvic pain.*

Response 2: To address the reviewer's comment, one sentence of the introduction was reworded as follows :

Psychosocial factors may also be involved in the development of LPP. Higher anxiety levels experienced in women who conceived after IVF might contribute to the higher pregnancy-related LPP prevalence observed in these women