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ABSTRACT

Objectives: Pregnancy-related pelvic girdle pain (PPGP) is a frequent condition known to significantly affect women's daily life. The etiology of PPGP is still not clearly established but the mode of conception has been suggested to contribute to PPGP. Anxiety related to fertility treatments may be one of the contributing factors. The primary objectives were to determine the evolution of PPGP prevalence and severity, and anxiety, throughout pregnancy in women who conceived spontaneously (SP) or after fertility treatments (FT). We also examined the relationship between PPGP severity and anxiety. The secondary objective was to determine the evolution of physical limitations and physical activity and their correlation with the severity of PPGP.

Design: Prospective cohort study.

Setting: Pregnant women were recruited through physicians' referrals, posters and newspaper advertisements in the local communities.

Participants: Fifty-nine pregnant women (33 SP and 26 FT) were assessed during the 1st, 2nd and 3rd trimester of pregnancy.

Primary and secondary outcome measures: PPGP prevalence and severity (primary), trait and state anxiety, physical limitations and physical activity levels (secondary).

Results: There was no relationship between the mode of conception and our outcomes. The prevalence and severity of PPGP increased over the course of pregnancy (time effect, $p<0.0001$) whereas trait anxiety decreased from early to mid-pregnancy (time effect, $p=0.03$). Physical limitations increased throughout pregnancy (time effect, $p<0.0001$) and physical activity levels decreased (time effect, $p<0.0001$). The severity of PPGP was positively correlated with physical limitations ($r=0.51$ to 0.55) but negatively with physical activity levels ($r= -0.39$ to -0.41).

Conclusions: Maternal health-related factors, such as PPGP, anxiety and physical activity, are not different in women who conceived spontaneously or after fertility treatments. The more PPGP was severe, the more the women were physically limited and inactive, suggesting that the clinical management of PPGP might decrease physical limitation during pregnancy. (299)

Strengths and limitations of this study

- This is a prospective cohort study of pregnant women who were assessed at each trimester of pregnancy, allowing to assess the evolution of several maternal health-related factors that are known to change over the course of pregnancy;
- Primary and secondary outcomes were collected using validated tools;
- One third of our sample achieved a pregnancy after *in vitro* fertilization, which may have limited our ability to find higher anxiety levels and PPGP incidence in women who conceived after fertility treatments compared to those who conceived naturally;
- More than half of the participants had a university degree and the results may not be generalizable to a wider population of pregnant women.

INTRODUCTION

Pregnancy-related pelvic girdle pain (PPGP) is defined by pain "experienced between the posterior iliac crest and the gluteal fold, particularly in the vicinity of the sacroiliac joint. The pain may radiate in the posterior thigh and can also occur in conjunction with/or separately in the symphysis" [1]. Using this definition, large prospective studies with objectively measured symptoms reported a PPGP prevalence between 16% and 25% [2]. The onset of PPGP varies considerably, between the end of the first trimester to the first month post-delivery, with a peak of symptoms generally occurring between the 24th and 36th weeks of pregnancy [2]. Pelvic girdle pain (PGP) is a debilitating condition during pregnancy that is known to affect women's quality of life. For instance, sleep, physical functioning, social life and hobbies are affected [3,4]. Importantly, PPGP represents the main cause of sick leave [5,6] and has therefore significant socioeconomic impact. Pregnant women experiencing PGP are also less likely to be physically active [7], thereby preventing them to benefit from the numerous positive health effects of prenatal exercise [8].

Several factors are believed to be involved in PPGP development [1,2]. One factor of interest is the mode of conception, in other words, naturally or after fertility treatments. A study reported that pregnant women who underwent *in vitro* fertilization (IVF) treatments had a two times higher prevalence rate of sacral pain in early and late pregnancy, as well as a higher prevalence of positive results on pelvic pain provocation tests in late pregnancy [9]. One of the reasons that might explain higher PPGP prevalence in women who conceived after IVF is higher anxiety levels. As reported by a systematic review, women who conceived following fertility treatments had greater pregnancy-specific anxiety than those who conceived naturally [10] and higher levels of anxiety have been found to be among the most notable factors associated with a higher likelihood of reporting PPGP [11]. However, additional studies are

needed to confirm the relationship between the mode of conception and PPGP, and whether anxiety is a contributing factor.

The primary objectives of this prospective cohort study were to determine the evolution of PPGP prevalence and severity, as well as anxiety, over the course of pregnancy in women who conceived naturally of after fertility treatments, and to examine the possible relationship between PPGP severity and anxiety levels. As PPGP has a significant impact on the women's daily life, the secondary objective of our study was to determine the evolution of physical limitations and physical activity behaviors throughout pregnancy and whether the severity of PPGP was correlated to these factors. Our primary hypotheses are that PPGP prevalence and severity, as well as anxiety levels will increase over the course of pregnancy but more strongly in women who conceived after fertility treatments, and that PPGP severity will be positively correlated with anxiety levels. As a result, our secondary hypotheses are that physical limitations will increase whereas physical activity behaviors will decrease over the course of pregnancy but more significantly in women who conceived after fertility treatments, and that the severity of PPGP will be positively correlated with physical limitations but negatively with physical activity behaviors.

MATERIALS AND METHODS

Study design and participants' selection

Between October 2015 and September 2016, women who achieved a spontaneous pregnancy (SP group) and women who achieved pregnancy following fertility treatments (FT group) were recruited through physicians' referrals, posters and newspaper advertisements in the local and surrounding communities. Women under 14 weeks of gestation, with a singleton pregnancy and able to understand, speak and write French were considered eligible to participate in the study. The study was approved by the local Research Ethics Committees

(CER-2015-003 and CER-15-214-07.10) and all participants provided their written informed consent.

Outcome measures and measurement tools

Women were followed from the 1st trimester of pregnancy until delivery through three evaluations (1st trimester [TR1]: 10–16 weeks, 2nd trimester [TR2]: 24–28 weeks and 3rd trimester [TR3]: 32–36 weeks of gestation). In each trimester, women were asked if they have had PPGP over the last 7 days or were having PPGP presently. If a woman had had or was having PPGP, she was asked to evaluate pain intensity using a visual analog pain scale (VAS). This scale is a self-reported measurement tool used by health professionals allowing the patient to rate pain from 0 (no pain) to 10 (extreme pain) [12]. We used a picture to localize the woman's pain to make sure that it was located in the lumbo-pelvic region.

The levels of anxiety was assessed during TR1, TR2 and TR3 using the French-Canadian version [13] of the State-Trait Anxiety Inventory (STAI) [14]. It is a self-reported questionnaire assessing the presence and severity of current symptoms of anxiety (state anxiety scale) and a generalized propensity to be anxious (trait anxiety scale). Each scale is based on 20 items on a four-point response scale. The range of score for each scale is 20-80, the higher score indicating greater anxiety levels.

Physical limitations and symptoms associated with PPGP were assessed in TR2 and TR3 using the completed the French-Canadian version of the PGQ was used [15]. The PGQ is a condition-specific measure developed for pregnant and postpartum women. It consists of 20 activity items and five symptom items on a four-point response scale and assess physical limitations and symptoms associated with PGP. The range of score is 0-100%, with a higher score indicating greater physical limitations and symptoms. The PGQ is reliable and valid for both pregnant and postpartum women with PGP [16].

Finally, physical activity levels were objectively measured at each trimester of pregnancy using the ActiGraph GT3X (ActiGraph, Pensacola, FL), a triaxial accelerometer measuring data in a 60-s epoch. The women were instructed to wear the monitor over the hip on an elastic belt for seven consecutive days from wake-up time to bedtime. They were allowed to remove the accelerometer when sleeping, showering or engaging in water activities. According to the method used in the Canadian Health Measures Survey, valid data were defined as ≥ four days of monitoring for ≥ 10 hours of wear time per day [17]. Pregnant women were encouraged to maintain their usual activities. Data were processed using the Actilife software version 6.13.2 (ActiGraph, LLC, FL, USA). The accelerometer data obtained were averaged across valid wear days. To derive the activity frequency, intensity and duration of the measured activity in counts per minute per day, the Freedson equation was used: sedentary (<100 counts), light (100–1951 counts), moderate (1952–5724), vigorous (5725–9498), and very vigorous (>9498) [18], as previously used in pregnant women [19]. Non-wear time was defined as a period of zero counts for ≥ 60 consecutive minutes, admitting a maximum of two consecutive minutes between 1 and 100 counts/min. When a third observation was between 1 and 100 counts or one observation was more than 100 counts, the non-wear period was ended. Bouts of moderate-to-vigorous physical activity (MVPA) was defined as a minimum of 10 consecutive minutes above 1952 counts and ended with more than two consecutive records below this threshold.

Patient and Public Involvement

Patients and public were not involved in the design and conduct of this study. The results will not be disseminated to study participants.

Statistical analysis

Means and standard deviations, as well as percentages, were computerized for variables of

interest. Student t-test was used to compare socio-demographic and anthropometric characteristics between SP and FT women. For categorical variables, the χ square test was used. Analysis of variance (ANOVA) for repeated measures was used to assess the evolution of the severity of PPGP, anxiety levels, physical limitations and physical activity behaviors throughout pregnancy in SP and FT women. To test whether the severity of PPGP was correlated to the levels of anxiety, physical limitations and physical activity behaviors at each trimester of pregnancy, Pearson's correlation analyses were used. Finally, exploratory logistic regression analyses were conducted to identify potential predictors of PPGP in TR3. Statistical analyses were performed by using the SAS software (version 9.4) and the level of significance was set to *p-value* ≤ 0.05.

RESULTS

Between October 2015 and May 2016, the study was presented to 117 eligible pregnant women, among which 62 women accepted to participate. Three women (1 in SP group and 2 in FT group) were excluded due to several missing data, leaving 59 women (33 SP and 26 FT) for the statistical analyses.

The characteristics of pregnant women are presented in **Table 1**. No significant difference in socio-demographic and pre-pregnancy anthropometric characteristics was found between the groups ($p>0.05$). Women were on average in their early thirties and approximately half of them were nulliparous. More than half were of normal weight pre-pregnancy (BMI 18.5-24.9 kg/m^2) and had a university degree. Women's PGP history, related or not to a previous pregnancy, was also similar between the groups, with approximately 50% of the women reporting a history of PGP (**Table 1**). Finally, the prevalence and severity of PPGP, anxiety and physical activity levels were not different between SP and FT pregnant women at study entry (**Table 1**). Data showed that on average, women considered PPGP as uncomfortable

(4/10) and were slightly anxious (35/80). Moreover, based on daily steps and physical activity recommendations [20,21], our population was considered inactive.

The prevalence of PPGP was similar in both groups during each trimester of pregnancy (TR1: $\chi^2 = 2.19$, p=0.33; TR2: $\chi^2 = 2,13$, p=0.33; TR3: $\chi^2 = 0.01$, p=0.92); the pooled prevalence of PPGP increased from 42% during TR1 to 65% during TR2 to 68% during TR3 ($\chi^2 = 8.45$; p=0.01) (**Fig 1**). Among women presenting PPGP at one time point during pregnancy (n=44, 26 SP and 18 FT), pain severity significantly increased over the course of pregnancy in both groups (time effect, p<0.0001. **Fig 2**), with pain severity being significantly higher during TR2 and TR3 compared to TR1. Trait anxiety decreased over the course of pregnancy in both groups (time effect, p<0.03. **Fig 3A**), with lower levels during TR2 compared to TR1, whereas state anxiety did not significantly change (**Fig 3B**). Finally, physical limitations associated with PPGP increased (time effect, p<0.0001. **Fig 4A**) whereas daily steps decreased over the course of pregnancy in both groups (time effect, p<0.0001. **Fig 4B).** The only time by group interaction effect was found for daily MVPA which decreased only in SP women (time effect, p<0.0001; time*group interaction effect, p=0.04. **Fig 4C).**

Since changes in the severity of PPGP, levels of anxiety, physical limitations and physical activity behaviors were similar between the groups, result from SP and FT women were pooled in the correlation analyses. Among women who presented PPGP, no correlation was found during TR1 between the severity of PPGP and anxiety or physical activity levels. During TR2, the severity of PPGP was positively correlated with physical limitations (r=0.51, p=0.001, **Fig 5A**) but negatively with daily steps (r=-0.39, p=0.03, **Fig 5B).** No correlation was found with daily MVPA **(Fig 5C).** During TR3, we found a positive correlation between the severity of PPGP and physical limitations (r=0.55, p=0.0002, **Fig 6A**) but a negative correlation with daily MVPA (r=-0.41, p=0.02, **Fig 6B**). No correlation was found with daily steps **(Fig 6C).**

Finally, exploratory logistic analyses revealed that among the potential predictors of PPGP during TR3 (mode of conception, parity, pre-pregnancy BMI, PPGP, anxiety and physical activity levels during TR1, and weight gain until TR3), PPGP during TR1 was the only significant predictor (odds ratio: 7.33, 95% confidence interval 1.82–29.48, p=0.005).

DISCUSSION

To the best of our knowledge, this is the first cohort study assessing the course of PPGP prevalence and severity in pregnant women who conceived naturally and after fertility treatments, and possible association with anxiety levels and physical activity behaviors. Overall, our primary results showed no relationship between the mode of conception and PPGP prevalence and severity, or anxiety levels. As expected, the prevalence and severity of PPGP increased over the course of pregnancy, whereas anxiety levels decreased from early to mid-pregnancy and were not correlated to the severity of PPGP.

Only one study examined the evolution of the prevalence and severity of PPGP according to the mode of conception. This study was conducted in 31 women who conceived after IVF and 200 women who conceived spontaneously and assessed PPGP at 12, 24 and 34 weeks of pregnancy [9]. The authors found an increase in PPGP prevalence and severity over the course of pregnancy in all women, as we and other authors did [22]. However, they reported a two times higher rate of PPGP in early and late pregnancy in women who achieved a pregnancy after IVF compared to those who achieved a pregnancy naturally but similar severity of PPGP [9]. Our hypothesis was that higher anxiety levels reported in women who conceived after fertility treatments [10] would contribute to higher PPGP prevalence and severity in this population of pregnant women. However, we did not find any difference in anxiety levels between women who conceived after fertility treatments and those who conceived naturally. Several reasons may explain our result. First, the majority of women included in our sample conceived after ovarian stimulation (OS, n=7) or intrauterine insemination (IUI, n=12), whereas the majority of studies included in Gourounti's review reporting higher anxiety in women who conceived following fertility treatments were conducted in the context of IVF [10]. It is very likely that OS and IUI generate less anxiety than IVF treatments, which might explain why we found no differences in anxiety levels in our sample. Second, the

questionnaire we used evaluated state and trait anxiety whereas Gourounti's review reported on pregnancy-specific anxiety [10]. It is possible that fertility treatments specifically affect anxiety related to pregnancy but not general anxiety, in which case the questionnaire we used may not have been specific enough to identify differences in anxiety between women who conceived after fertility treatment and those who conceived naturally.

When examining anxiety levels over the course of pregnancy, we found a U-shaped curve, with a significant decrease in anxiety from TR1 to TR2 and a non-significant trend toward an increase from TR2 to TR3. These findings are similar to those of previous studies [23,24]. In contrast, whereas some studies reported higher anxiety in pregnant women with PPGP [11,25], we found no correlation between anxiety levels and PPGP severity. Our findings suggest that in our sample, anxiety and PPGP were two independent phenomena.

Likewise, our secondary results showed no relationship between the mode of conception and physical limitations and physical activity behaviors, except for MVPA during TR3. The decrease in MVPA observed only in women who conceived naturally needs further investigation. Similarly to previous studies [26-29], we found that with advancing pregnancy, physical limitations increased [28-30] and physical activity behaviors decreased [26,27,31]. Our data further showed that the greater PPGP severity the greater physical limitation and lower physical activity levels in mid- and late pregnancy. These results are also in accordance with previous studies reporting decreased physical activity levels as physical limitations and low back pain increase with advancing pregnancy [28,32].

Despite the high prevalence of PPGP, little is known about the risk factors for PPGP. Clinical management would benefit from an early identification of women at risk of developing PPGP later in pregnancy. Exploratory univariate logistic regression analyses were carried out and revealed that the presence of PPGP during TR1 was a significant predictor of PPGP in TR3. This finding is in accordance with those of Robinson et al. [29] who reported an association

between pain and positive pain provocation test in early pregnancy and disability and pain intensity in late pregnancy.

Limitations

The current study has a few limitations that should be acknowledged. First, as previously mentioned, our sample was heterogeneous with regards to fertility treatments used to achieve a pregnancy, with the majority of women having conceived after OS or IUI. This may have limited our ability to find higher PPGP prevalence and anxiety levels in women who conceived after fertility treatments. Third, general anxiety was assessed whereas the type of anxiety that may be influenced by the mode of conception may be more specific to pregnancy. We had missing physical activity data, suggesting that several women did not wear the accelerometer for at least 10 hours per day for four days. Some women with PPGP reported discomfort when wearing the accelerometer, suggesting that we may have under-evaluated physical activity levels. Finally, more than half of the women we recruited had a university degree. This suggests a possible recruitment bias and limits the generalizability of our results to a wider population of pregnant women. However, the strength of our study is its longitudinal design that allowed us to examine the evolution of several maternal health-related factors that are known to change over the course of pregnancy. Moreover, our study clarifies the relationship between PPGP severity and physical activity behaviors using accelerometers, which is an objective measurement tool frequently used in pregnant women to assess physical activity levels and sedentary behaviors [19].

CONCLUSION

In conclusion, our findings suggest that maternal health-related factors, such as PPGP, anxiety and physical activity behaviors, are not different in women who conceived after fertility treatments and those who conceived spontaneously. The lack of correlation between PPGP severity and anxiety levels suggests that they are two independent phenomena. The increase in PPGP severity and physical limitations, and decrease in physical activity behaviors with advancing gestation, and the fact that the more severe PPGP the greater physical limitations and physical inactivity in mid- and late pregnancy underlie the importance of PPGP management to allow pregnant women performing their daily activities.

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Declaration of conflicting interests: The authors declare that there is no conflict of interest.

Author Contributions: SMR, MD, VB contributed to the study concept and design; EL and AStL acquired the data; SMR, MD, EL performed the statistical analysis and interpreted the data; EL and SMR drafted the manuscript; MD, AStL and VB critically reviewed the manuscript for important intellectual content. All authors read and approved the final manuscript.

Competing interests: None declared.

Ethics approval: The study was approved by the local Research Ethics Committees (CER-2015-003 and CER-15-214-07.10)

Data sharing statement: No additional data are available.

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Table 1: Baseline characteristics of the 59 pregnant women included in study.

Variables	FT (n=26) Means ±SD	SP (n=33) Means ±SD	P values
Fertility treatments	OS=7 IUI=12 IVF=7	-	
Age (years)	32.2 ±3.6	30.9 ± 4.2	0.23
Parity	0.4 ± 0.6	0.6 ± 0.6	0.36
0 (n)	57.7% (15)	45.5% (15)	0.35
≥1 (n)	42.3% (11)	54.6% (18)	
Pre-pregnancy BMI (kg/cm^2)	26.3± 7.3	25.2 ± 6.6	0.54
Underweight <18.4	0% (0)	3.1% (1)	0.81
Normal weight (18.5-24.9)	60.0 (15)	62.5% (20)	
Overweight (25.0-29.9)	20.0 (5)	18.8% (6)	
Obese ≥30.0	20.0%(5)	15.6% (5)	
Education levels			
Non-university degree	42.3% (11)	33.3% (11)	0.48
University degree	57.7% (15)	66.7% (22)	
PGP history (yes) [1]	46.2% (12)	54.6% (18)	0.52
Prevalence of PGP over the last week (yes)	34.6% (9)	48.5% (16)	0.33
Severity of PGP over the last week	2.9 ± 1.9	4.1± 2.3	0.18
State anxiety	37.4 ± 11.6	34.2 ± 9.1	0.28
Trait anxiety	39.8 ± 10.0	37.1 ± 9.4	0.26
Daily steps	5328 ± 1551	5569 ± 1552	0.80
Daily MVPA (min)	16.3 ± 10.0	17.4 ± 13.2	0.97

FT: fertility treatment; SP: spontaneous conception; OS: ovarian stimulation; IUI: intrauterine insemination; IVF: *in vitro* fertilization; BMI : body mass index; PGP : pelvic girdle pain; MVPA: moderate-to-vigorous physical activity

[1] PGP history includes history of pregnancy-related PGP and PGP not related to pregnancy

Missing data: pre-pregnancy BMI: 1 FT, 1 SP; state and trait anxiety : 1 SP; accelerometer data: 4 SP; 6 FT

Figure legend

Figure 1: Prevalence of PPGP in FT and SP pregnant women over the course of pregnancy.

Figure 2: Evolution of PPGP severity in FT and SP pregnant women over the course of pregnancy.

Figure 3: Evolution of (A) trait anxiety and (B) state anxiety in FT and SP pregnant women over the course of pregnancy.

Figure 4: Evolution of (A) physical limitations, (B) daily step counts an (C) daily moderate-to-vigorous physical activity in FT and SP pregnant women over the course of pregnancy.

Figure 5: Correlation between the severity of PPGP and (A) physical limitations, (B) daily step counts and (C) daily moderate-to-vigorous physical activity at TR2.

Figure 6: Correlation between the severity of PPGP and (A) physical limitations, (B) daily step counts and (C) daily moderate-to-vigorous physical activity at TR3.

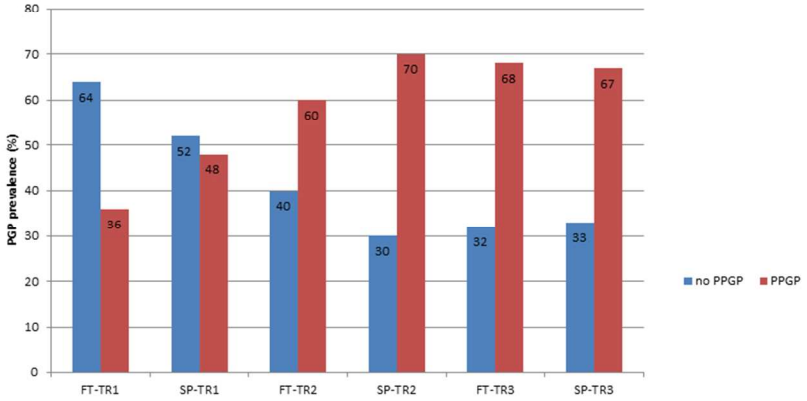

Figure 1: Prevalence of PPGP in FT and SP pregnant women over the course of pregnancy.

254x190mm (96 x 96 DPI)

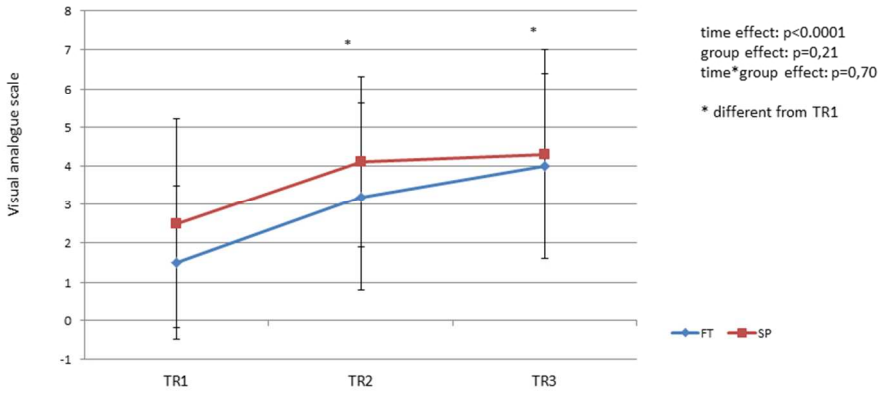

Figure 2: Evolution of PPGP severity in FT and SP pregnant women over the course of pregnancy.

254x190mm (96 x 96 DPI)

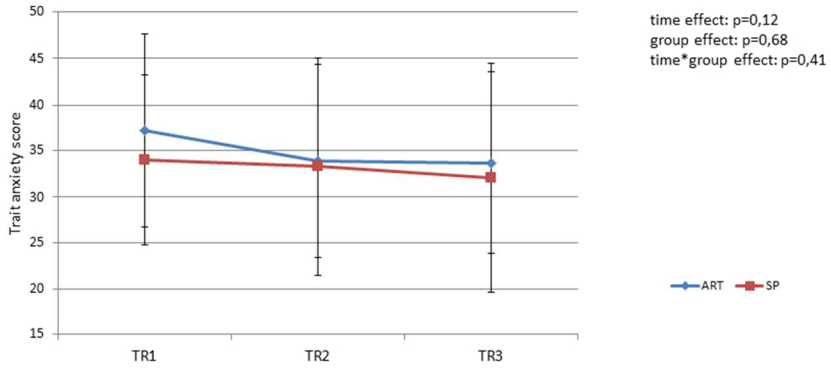

Figure 3: Evolution of trait anxiety in FT and SP pregnant women over the course of pregnancy.

254x190mm (96 x 96 DPI)

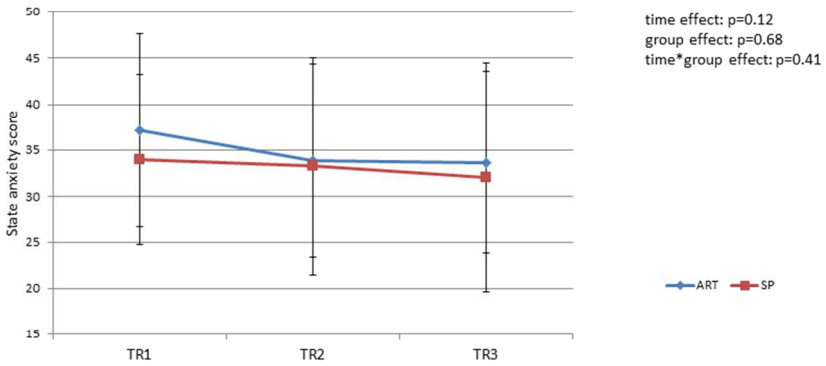

Figure 3: Evolution of state anxiety in FT and SP pregnant women over the course of pregnancy.

254x190mm (96 x 96 DPI)

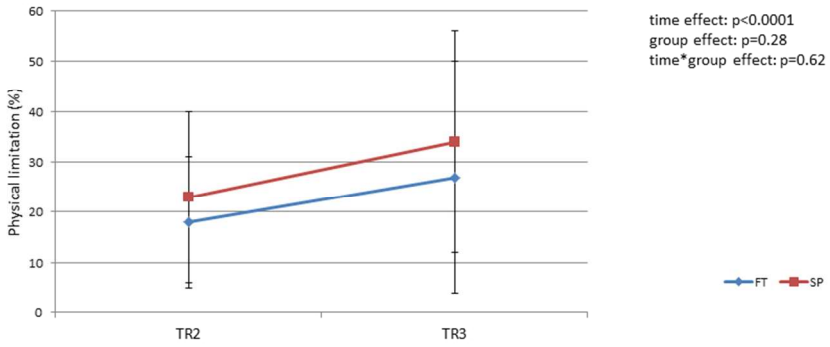

Figure 4: Evolution of physical limitations in FT and SP pregnant women over the course of pregnancy.

254x190mm (96 x 96 DPI)

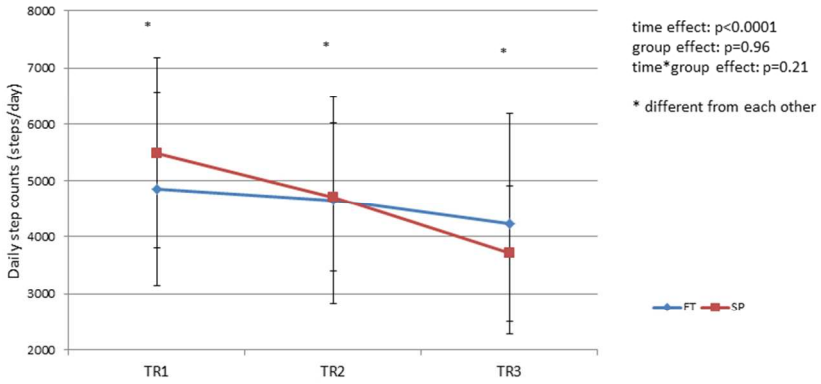

Figure 4: Evolution of daily step counts in FT and SP pregnant women over the course of pregnancy.

254x190mm (96 x 96 DPI)

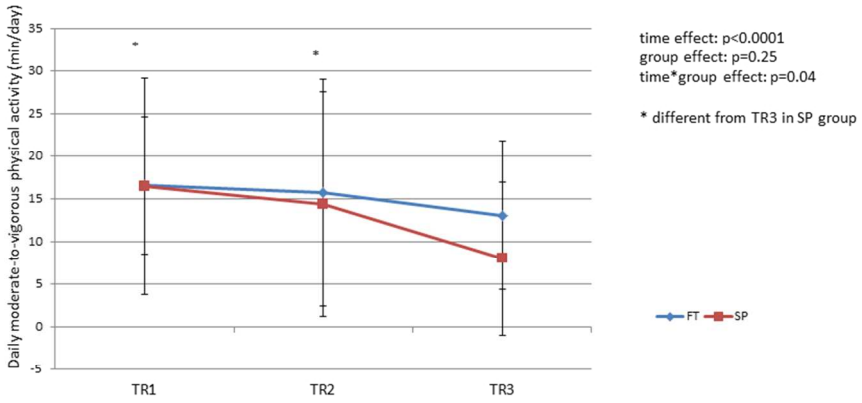

Figure 4: Evolution of daily moderate-to-vigorous physical activity in FT and SP pregnant women over the course of pregnancy.

254x190mm (96 x 96 DPI)

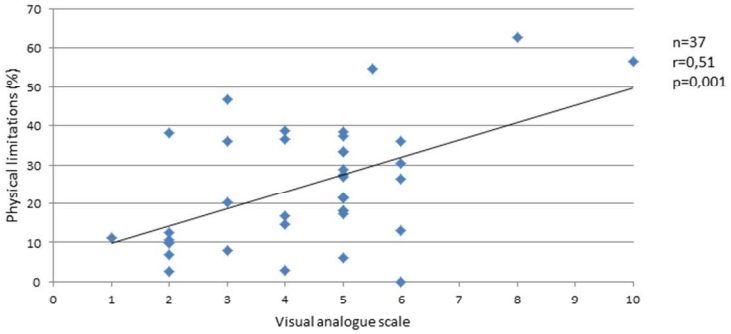

Figure 5: Correlation between the severity of PPGP and physical limitations at TR2.

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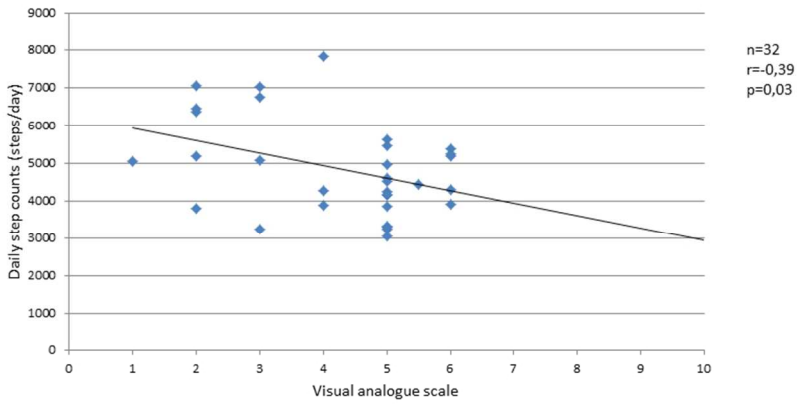

Figure 5: Correlation between the severity of PPGP and daily step counts at TR2.

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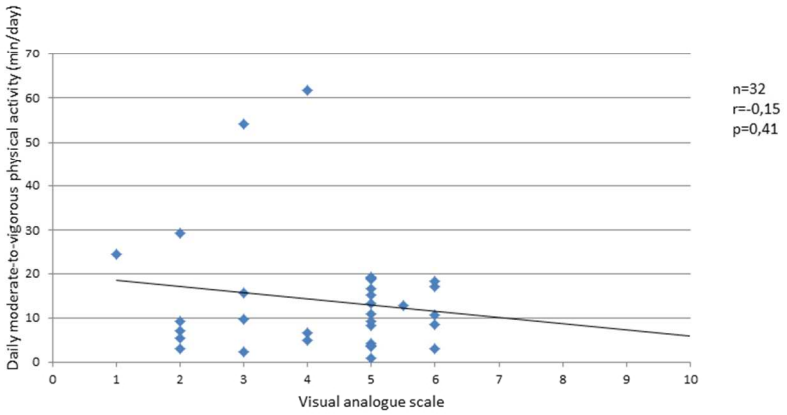

Figure 5: Correlation between the severity of PPGP and daily moderate-to-vigorous physical activity at TR2.

254x190mm (96 x 96 DPI)

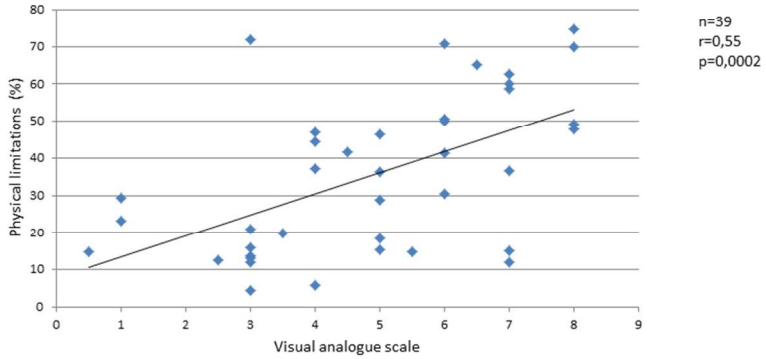

Figure 6: Correlation between the severity of PPGP and physical limitations at TR3.

254x190mm (96 x 96 DPI)

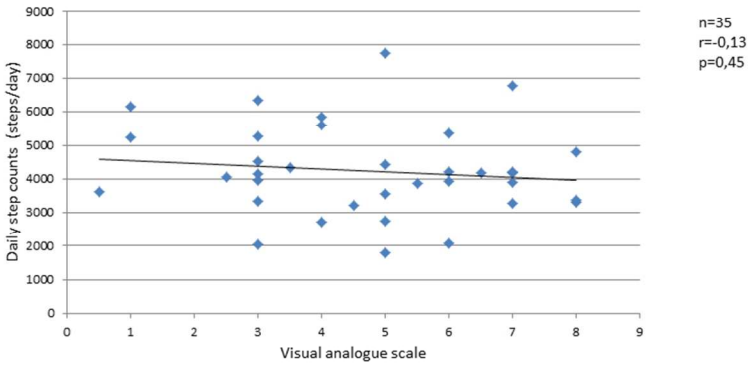

Figure 6: Correlation between the severity of PPGP and daily step counts at TR3.

254x190mm (96 x 96 DPI)

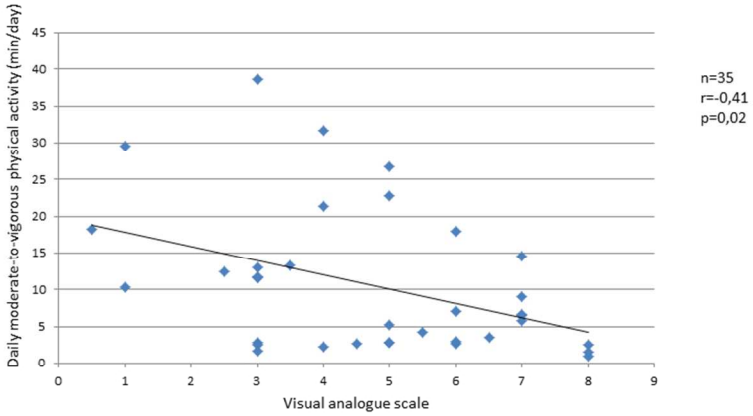

Figure 6: Correlation between the severity of PPGP and daily moderate-to-vigorous physical activity at TR3.

254x190mm (96 x 96 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	na
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	-
Study size	10	Explain how the study size was arrived at	-
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	na
		(*d*) If applicable, explain how loss to follow-up was addressed	na
		(*e*) Describe any sensitivity analyses	na
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8, 19 (table 1)
		(b) Indicate number of participants with missing data for each variable of interest	na
		(c) Summarise follow-up time (eg, average and total amount)	6
Outcome data	15*	Report numbers of outcome events or **summary measures over time**	8-9, 20-28 (figures)
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	na
		(*b*) Report category boundaries when continuous variables were categorized	na
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	na
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	na
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-11
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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

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Manuscript title: Lumbopelvic pain, anxiety, physical activity and mode of conception: A prospective cohort study of pregnant women

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ABSTRACT

Objectives: Pregnancy-related lumbopelvic pain (LPP) is a frequent condition known to significantly affect women's daily life. The etiology of pregnancy-related LPP pain is still not clearly established but the mode of conception has been suggested to contribute LPP. Anxiety related to fertility treatments may be one of the contributing factors. The primary objectives were to determine the evolution of LPP prevalence and severity, and anxiety, throughout pregnancy in women who conceived spontaneously (SP) or after fertility treatments (FT). A further aim was to examine the relationship between pregnancy-related LPP severity and anxiety. The secondary objective was to determine the evolution of physical activity and their correlation with the severity of pregnancy-related LPP.

Design: Prospective cohort study.

Setting: Pregnant women were recruited through physicians' referrals, posters and newspaper advertisements in the local and surrounding communities (hospital, maternity care clinic, prenatal centers, sports centers, local university).

Participants: Fifty-nine pregnant women (33 SP and 26 FT) were assessed during the 1st, 2nd and 3rd trimester of pregnancy.

Primary and secondary outcome measures: Pregnancy-related LPP prevalence and severity (primary), trait and state anxiety, and physical activity levels (secondary).

Results: There was no relationship between the mode of conception and the outcome measures. The prevalence and severity of LPP increased over the course of pregnancy (time effect, $p<0.0001$) whereas trait anxiety decreased from early to mid-pregnancy (time effect, $p=0.03$). Activity limitations increased throughout pregnancy (time effect, $p<0.0001$) and physical activity levels decreased (time effect, $p<0.0001$). The severity of LPP was positively correlated with activity limitations ($r=0.51$ to 0.55) but negatively with physical activity levels ($r= -0.39$ to -0.41).

Conclusions: Maternal health-related factors, such as LPP, anxiety and physical activity, are not different in women who conceived spontaneously or after fertility treatments. The more LPP was severe, the more the women were physically limited and inactive.

Strengths and limitations of this study

- This is a prospective cohort study of pregnant women who were assessed at each trimester of pregnancy, allowing to determine the evolution of several maternal health-related factors that are known to change over the course of pregnancy;
- Primary and secondary outcomes were collected using validated tools;
- The low number of women who achieved a pregnancy following *in vitro* fertilization prevented us to fully test our hypotheses; thus larger studies are needed to better understand whether IVF contribute to pregnancy-related LPP.
- More than half of the participants had a university degree, which is not representative of our local population. The results may therefore not be broadly generalizable.

INTRODUCTION

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 the different periods during pregnancy LPP was assessed. The onset of LPP varies considerably, between the end of the first trimester to the first month post-delivery, with a peak of symptoms generally occurring between the 24th and 36th weeks of pregnancy [6]. 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]. 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].

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]. Another factor of interest is the mode of conception, in other words, naturally or after fertility treatments. A study reported that pregnant women who underwent *in vitro* fertilization (IVF) treatments had a two times higher prevalence rate of sacral pain in early

and late pregnancy, as well as a higher frequency of positive results on pelvic pain provocation tests in late pregnancy [15]. The authors concluded that relaxin causes pelvic pain because relaxin is higher in IVF pregnancies [16]. Another reason that might explain higher pregnancy-related LPP prevalence in women who conceived after IVF is higher anxiety levels. As reported by a systematic review, women who conceived following fertility treatments had greater pregnancy-specific anxiety than those who conceived naturally[17]. Based on a multi-center study including 1,158 women, higher levels of anxiety was reported to be among the most notable factors associated with a higher likelihood of reporting LBP [18]. However, to the best of our knowledge, no study has examined pregnancy-related LPP among women who achieve pregnancy naturally or after fertility treatment, and whether anxiety is a contributing factor to the development of LPP.

The primary objectives of this prospective cohort study were to determine the evolution of LPP prevalence and severity, as well as anxiety, over the course of pregnancy in women who conceived naturally or after fertility treatments, and to examine the possible relationship between pregnancy-related LPP severity and anxiety levels. As pregnancy-related LPP has a significant impact on the women's daily life, the secondary objective of our study was to determine the evolution of physical activity behaviors throughout pregnancy and whether the severity of LPP was correlated to these factors. Our primary hypotheses are that LPP prevalence and severity, as well as anxiety levels will increase over the course of pregnancy but more strongly in women who conceived after fertility treatments, and that pregnancy-related LPP severity will be positively correlated with anxiety levels. As a result, our secondary hypotheses are that activity limitations will increase whereas physical activity behaviors will decrease over the course of pregnancy but more significantly in women who conceived after fertility treatments, and that the severity of pregnancy-related LPP will be positively correlated with activity limitations but negatively with physical activity behaviors.

MATERIALS AND METHODS

Study design and participants' selection

This is a prospective cohort study of pregnant women who were recruited between October 2015 and September 2016. 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). Women under 14 weeks of gestation, with a singleton pregnancy and able to understand, speak and write French were considered eligible to participate in the study. The study was approved by the local Research Ethics Committees (CER-2015-003 and CER-15-214-07.10) and all participants provided their written informed consent.

Outcome measures and measurement tools

Women were followed from the 1st trimester of pregnancy until delivery through three evaluations (1st trimester [TR1]: 10–16 weeks, 2nd trimester [TR2]: 24–28 weeks and 3rd trimester [TR3]: 32–36 weeks of gestation). 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]. If a woman had or was having pregnancy-related LPP, she was asked to rate pain intensity using a visual analog pain scale (VAS). This scale is a self-reported measurement tool used by health professionals allowing the patient to rate pain from 0 (no pain) to 10 (extreme pain) [20].

The levels of anxiety was assessed during TR1, TR2 and TR3 using the French-Canadian version [21] of the State-Trait Anxiety Inventory (STAI) [22]. The STAI is a self-reported

questionnaire assessing the presence and severity of current symptoms of anxiety (state anxiety scale) and a generalized propensity to be anxious (trait anxiety scale). Each scale is based on 20 items on a four-point response scale. The range of score for each scale is 20-80, the higher score indicating greater anxiety levels. 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].

Activity limitations and symptoms associated with pregnancy-related LPP were assessed in TR2 and TR3 using the completed the French-Canadian version of the PGQ was used [19]. The PGQ is a condition-specific measure developed for pregnant and postpartum women. It consists of 20 activity items and five symptom items on a four-point response scale and assesses activity limitations and symptoms associated with pain in the lumbopelvic region. The range of score is 0-100%, with a higher score indicating greater activity limitations and symptoms. The PGQ is reliable and valid for both pregnant and postpartum women with pregnancy-related LPP [24].

Finally, physical activity levels were objectively measured at each trimester of pregnancy using the ActiGraph GT3X (ActiGraph, Pensacola, FL), a triaxial accelerometer measuring data in a 60-s epoch. The women were instructed to wear the monitor over the hip on an elastic belt for seven consecutive days from wake-up time to bedtime. They were allowed to remove the accelerometer when sleeping, showering or engaging in water activities. Furthermore, the women received a daily diary to document wear and non-wear time periods and water activities. According to the method used in the Canadian Health Measures Survey, valid data were defined as ≥ four days of monitoring for ≥ 10 hours of wear time per day [25]. Pregnant women were encouraged to maintain their usual activities. Data were processed using the Actilife software version 6.13.2 (ActiGraph, LLC, FL, USA). The accelerometer data obtained were averaged across valid wear days. To derive the activity frequency,

intensity and duration of the measured activity in counts per minute per day, the Freedson equation was used: sedentary (<100 counts), light (100–1951 counts), moderate (1952–5724), vigorous (5725–9498), and very vigorous (>9498) [26], as previously used in pregnant women [27]. Non-wear time was defined as a period of zero counts for ≥ 60 consecutive minutes, admitting a maximum of two consecutive minutes between 1 and 100 counts/min. When a third observation was between 1 and 100 counts or one observation was more than 100 counts, the non-wear period was ended. Bouts of moderate-to-vigorous physical activity (MVPA) was defined as a minimum of 10 consecutive minutes above 1952 counts and ended with more than two consecutive records below this threshold.

Patient and Public Involvement

Patients and public were not involved in the design and conduct of this study. The results will not be disseminated to study participants.

Statistical analysis

Means and standard deviations, as well as percentages, were computerized for variables of interest. Student t-test was used to compare socio-demographic and anthropometric characteristics between SP and FT women. For categorical variables, the χ square test was used. 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]). 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 a significant effect of time, group or interaction effect was found, post-hoc analyses were conducted using the Tukey test. To test whether the severity of pregnancy-related LPP was correlated to the levels of anxiety (objective 1), and

physical activity behaviors (objective 2) at each trimester of pregnancy, Pearson's correlation analyses were used. Statistical analyses were performed by using the SAS software (Institute, Cary, NC, version 9.4) and the level of significance was set to *p-value* ≤ 0.05.

RESULTS

Between October 2015 and September 2016, the study was presented by physicians or to 117 eligible pregnant women, among which 62 women accepted to participate. Reasons for not agreeing to participate to the study were lack of interest or lack of time. Three women (1 in SP group and 2 in FT group) were excluded due to loss to follow-up (n=1), miscarriage (n=1) or missing data (n=1), leaving 59 women (33 SP and 26 FT) for the statistical analyses.

The characteristics of pregnant women are presented in **Table 1**. No significant difference in socio-demographic and pre-pregnancy anthropometric characteristics was found between the groups (p>0.05). Women were on average in their early thirties and approximately half of them were nulliparous. More than half were of normal weight pre-pregnancy (BMI 18.5-24.9 kg/m^2) and had a university degree. Women's LPP history, related or not to a previous pregnancy, was also similar between the groups, with approximately 50% of the women reporting a history of LPP (**Table 1**). Finally, the prevalence and severity of pregnancy-related LPP, anxiety and physical activity levels were not different between SP and FT pregnant women at study entry (**Table 1**). Data showed that on average, women considered LPP as moderate (4/10) and were slightly anxious (35/80). Moreover, based on daily steps and physical activity recommendations [28 29], our population was considered inactive.

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. Furthermore, physical activity data was missing for 10

(17%), 7 (12%) and 8 (14%) women at TR1, TR2 and TR3, respectively, because those women did not wear the accelerometer for at least 10 hours per day for at least four days.

The prevalence of pregnancy-related LPP was similar in both groups during each trimester of pregnancy (TR1: $\chi^2 = 2.19$, p=0.33; TR2: $\chi^2 = 2.13$, p=0.33; TR3: $\chi^2 = 0.01$, p=0.92); the pooled prevalence increased from 42% during TR1 to 65% during TR2 to 68% during TR3 ($\chi^2 = 8.45$; p=0.01) (**Fig 1**). Among women presenting with pregnancy-related LPP at one time point during pregnancy (n=44, 26 SP and 18 FT), pain severity significantly increased over the course of pregnancy in both groups (time effect: F=14.81, p<0.0001. **Fig 2**), with pain severity being significantly higher during TR2 and TR3 compared to TR1. Trait anxiety decreased over the course of pregnancy in both groups (time effect: F=3.93, p<0.03. **Fig 3**), with lower levels during TR2 compared to TR1, whereas state anxiety did not significantly change (**Fig 4**). Finally, activity limitations associated with pregnancy-related LPP increased (time effect: F=18.82, p<0.0001. **Fig 5**) whereas daily steps decreased over the course of pregnancy in both groups (time effect: F=16.03, p<0.0001. **Fig 6).** The only time by group interaction effect was found for daily MVPA (time effect: F=13.11, p<0.0001; time*group interaction effect: F=3.38, p=0.04. **Fig 7),** with daily MVPA being lower in TR3 compared to TR1 and TR2 only in SP women.

Since changes in the severity of pregnancy-related LPP, levels of anxiety, and physical activity behaviors were similar between the groups, result from SP and FT women were pooled in the correlation analyses. Among women who presented with pregnancy-related LPP, no correlation was found during TR1 between the severity of pregnancy-related LPP and anxiety or physical activity levels. During TR2, the severity of pregnancy-related LPP was positively correlated with activity limitations (r=0.51, p=0.001, **Fig 8**) but negatively with daily steps (r=-0.39, p=0.03, **Fig 9).** No correlation was found with daily MVPA **(Fig 10).** During TR3, we found a positive correlation between the severity of pregnancy-related

LPP and activity limitations (r=0.55, p=0.0002, **Fig 11**) and a negative correlation with daily MVPA (r=-0.41, p=0.02, **Fig 12**). No correlation was found with daily steps **(Fig 13).**

DISCUSSION

To the best of our knowledge, this is the first cohort study assessing the course of pregnancy-related LPP prevalence and severity in pregnant women who conceived naturally and after fertility treatments, and possible association with anxiety levels and physical activity behaviors. Overall, our primary results showed no differences in LPP prevalence and severity, or anxiety levels between women who achieved a pregnancy naturally or after fertility treatments. 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]. Anxiety levels decreased from early to mid-pregnancy and were not correlated to the severity of LPP.

Only one study examined the evolution of the prevalence and severity of pregnancy-related PGP (PPGP) according to the mode of conception [15]. This study was conducted in 31 women who conceived after IVF and 200 women who conceived spontaneously and assessed PGP at 12, 24 and 34 weeks of pregnancy. The authors found an increase in PPGP prevalence and severity over the course of pregnancy in all women, as we and other authors did [30]. However, they reported a two times higher rate of PPGP in early and late pregnancy in women who achieved a pregnancy after IVF compared to those who achieved a pregnancy naturally but similar severity of PPGP [15]. 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.

Our hypothesis was that higher anxiety levels reported in women who conceived after fertility treatments [17] would contribute to higher pregnancy-related LPP prevalence and severity in

this population of pregnant women. However, we did not find any difference in anxiety levels between women who conceived after fertility treatments and those who conceived naturally. Several reasons may explain our result. First, the majority of women included in our sample conceived after ovarian stimulation (OS, n=7) or intrauterine insemination (IUI, n=12), whereas the majority of studies included in Gourounti's review reporting higher anxiety in women who conceived following fertility treatments were conducted in the context of IVF [17]. 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.

When examining anxiety levels over the course of pregnancy, we found a U-shaped curve, with a significant decrease in anxiety from TR1 to TR2 and a non-significant trend toward an increase from TR2 to TR3. These findings are similar to those of previous studies [31 32]. In contrast, whereas some studies reported higher anxiety in pregnant women with LBP or PGP [18 33], we found no correlation between anxiety levels and LPP severity. Our findings suggest that in our sample, anxiety and LPP were two independent phenomena.

Likewise, our secondary results showed no relationship between the mode of conception and physical limitations and physical activity behaviors, except for MVPA during TR3. The decrease in MVPA observed only in women who conceived naturally needs further investigation. Similarly to previous studies [34-37], we found that with advancing pregnancy, physical limitations increased [36-38] and physical activity behaviors decreased [34 35 39]. Our data further showed that the greater pregnancy-related LPP severity the greater physical limitation and lower physical activity levels in mid- and late pregnancy. These results are also in accordance with previous studies reporting decreased physical activity levels as physical limitations and low back pain increase with advancing pregnancy [36 40].

Limitations

The strength of our study is its longitudinal design that allowed us to examine the evolution of several maternal health-related factors that are known to change over the course of pregnancy, in the context of spontaneous pregnancies and pregnancies achieved following FT. Moreover, our study adds knowledge about the relationship between pregnancy-related LPP severity and physical activity behaviors. However, the current study has limitations that should be acknowledged. First, our sample was heterogeneous with regards to fertility treatments used to achieve a pregnancy, with the majority of women having conceived after OS or IUI. This may explain the lower prevalence of PPGP and anxiety levels in women who conceived after fertility treatments. 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. Second, more than half of the women we recruited had a university degree, which is more than in our local population (22.5%) [41]. This suggests a possible recruitment bias and limits the generalizability of our results. 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. We also had missing physical activity data because some women did not wear the accelerometer for at least 10 hours per day for at least four days. 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 do not 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.

CONCLUSION

In conclusion, our findings suggest that maternal health-related factors, such as LPP, anxiety and physical activity behaviors, are not different in women who conceived after fertility treatments and those who conceived spontaneously. The lack of correlation between the severity of pregnancy-related LPP and anxiety levels suggests that they are two independent phenomena. The increase in LPP severity and activity limitations, and decrease in physical activity behaviors with advancing gestation, and the fact that the more severe LPP the greater activity limitations and physical inactivity in mid- and late pregnancy underline the importance of pregnancy-related LPP management to allow pregnant women performing their daily activities.

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Declaration of conflicting interests: The authors declare that there is no conflict of interest.

Author Contributions: SMR, MD, VB contributed to the study concept and design; EL and AStL acquired the data; SMR, MD, EL performed the statistical analysis and interpreted the data; EL and SMR drafted the manuscript; MD, AStL and VB critically reviewed the manuscript for important intellectual content. All authors read and approved the final manuscript.

Competing interests: None declared.

Ethics approval: The study was approved by the local Research Ethics Committees (CER-2015-003 and CER-15-214-07.10)

Data sharing statement: No additional data are available.

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Table 1: Baseline characteristics of the 59 pregnant women included in study.

Variables	FT (n=26) Means ±SD	SP (n=33) Means ±SD	P values
Fertility treatments	OS=7 IUI=12 IVF=7	-	
Age (years)	32.2 ±3.6	30.9 ± 4.2	0.23
Parity	0.4 ± 0.6	0.6 ± 0.6	0.36
0 (n)	57.7% (15)	45.5% (15)	0.35
≥1 (n)	42.3% (11)	54.6% (18)	
Pre-pregnancy BMI (kg/cm^2)	26.3± 7.3	25.2 ± 6.6	0.54
Underweight <18.4	0% (0)	3.1% (1)	0.81
Normal weight (18.5-24.9)	60.0 (15)	62.5% (20)	
Overweight (25.0-29.9)	20.0 (5)	18.8% (6)	
Obese ≥30.0	20.0%(5)	15.6% (5)	
Education levels			
Non-university degree	42.3% (11)	33.3% (11)	0.48
University degree	57.7% (15)	66.7% (22)	
LPP history (yes) [1]	46.2% (12)	54.6% (18)	0.52
Prevalence of pregnancy-related LPP over the last week (yes)	34.6% (9)	48.5% (16)	0.33
Severity of pregnancy-related LPP over the last week	2.9 ± 1.9	4.1± 2.3	0.18
State anxiety	37.4 ± 11.6	34.2 ± 9.1	0.28
Trait anxiety	39.8 ± 10.0	37.1 ± 9.4	0.26
Daily steps	5328 ± 1551	5569 ± 1552	0.80
Daily MVPA (min)	16.3 ± 10.0	17.4 ± 13.2	0.97

FT: fertility treatment; SP: spontaneous conception; OS: ovarian stimulation; IUI: intrauterine insemination; IVF: *in vitro* fertilization; BMI : body mass index; LPP : lumbopelvic pain; MVPA: moderate-to-vigorous physical activity

[1] LPP history includes history of pregnancy-related LPP and LPP not related to pregnancy

Missing data: pre-pregnancy BMI: 1 FT, 1 SP; state and trait anxiety : 1 SP; accelerometer data: 4 SP; 6 FT

Figure legend

Figure 1: Prevalence of pregnancy-related lumbopelvic pain (LPP) in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

Figure 1 footnote: TR1: 1st trimester of pregnancy; TR2: 2nd trimester of pregnancy; TR3: 3rd trimester of pregnancy.

Figure 2: Evolution of pregnancy-related lumbopelvic pain (LPP) severity in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

Figure 2 footnote: TR1: 1st trimester of pregnancy; TR2: 2nd trimester of pregnancy; TR3: 3rd trimester of pregnancy.

Figure 3: Evolution of trait anxiety in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

Figure 3 footnote: TR1: 1st trimester of pregnancy; TR2: 2nd trimester of pregnancy; TR3: 3rd trimester of pregnancy.

Figure 4: Evolution of state anxiety in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

Figure 4 footnote: TR1: 1st trimester of pregnancy; TR2: 2nd trimester of pregnancy; TR3: 3rd trimester of pregnancy.

Figure 5: Evolution of activity limitations in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

Figure 5 footnote: TR1: 1st trimester of pregnancy; TR2: 2nd trimester of pregnancy; TR3: 3rd trimester of pregnancy.

Figure 6: Evolution of daily moderate-to-vigorous physical activity (MVPA) in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

Figure 6 footnote: TR1: 1st trimester of pregnancy; TR2: 2nd trimester of pregnancy; TR3: 3rd trimester of pregnancy.

Figure 7: Evolution of daily step counts in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

Figure 7 footnote: TR1: 1st trimester of pregnancy; TR2: 2nd trimester of pregnancy; TR3: 3rd trimester of pregnancy.

Figure 8: Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and activity limitations in the 2nd trimester of pregnancy (TR2).

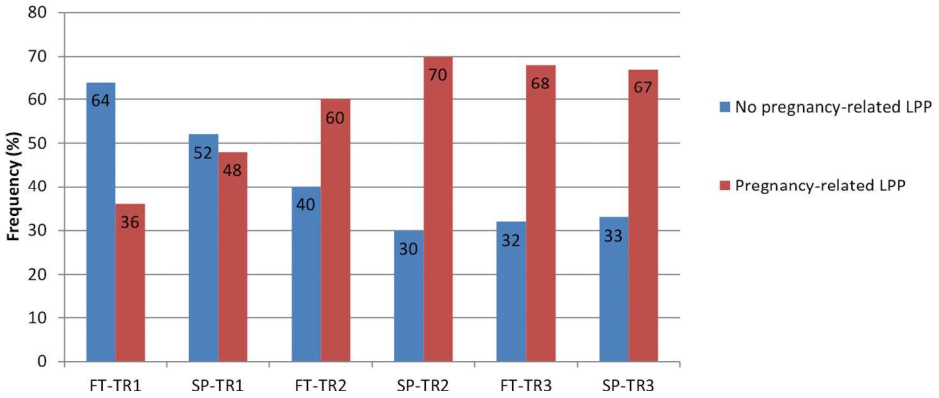
Figure 9: Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and daily moderate-to-vigorous physical activity (MVPA) in the 2nd trimester of pregnancy (TR2).

Figure 10: Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and daily step counts in the 2nd trimester of pregnancy (TR2).

Figure 11: Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and activity limitations in the 3rd trimester of pregnancy (TR3).

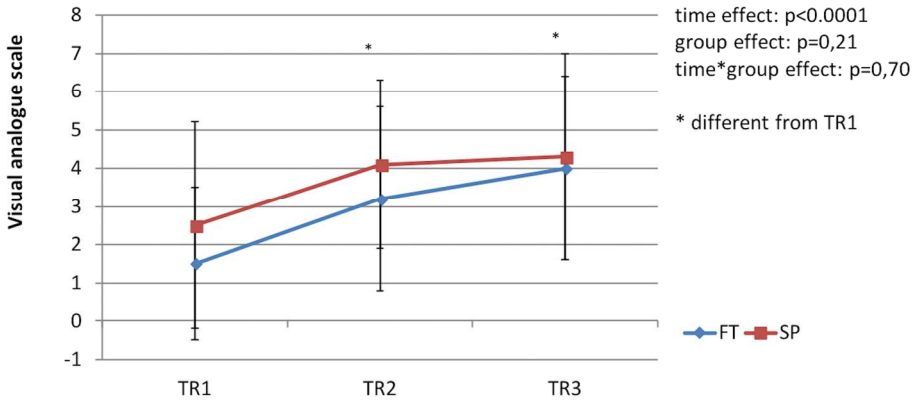
Figure 12: Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and daily moderate-to-vigorous physical activity (MVPA) in the 3rd trimester of pregnancy (TR3).

Figure 13: Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and daily step counts in the 3rd trimester of pregnancy (TR3).



Prevalence of pregnancy-related lumbopelvic pain (LPP) in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

263x132mm (300 x 300 DPI)



Evolution of pregnancy-related lumbopelvic pain (LPP) severity in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

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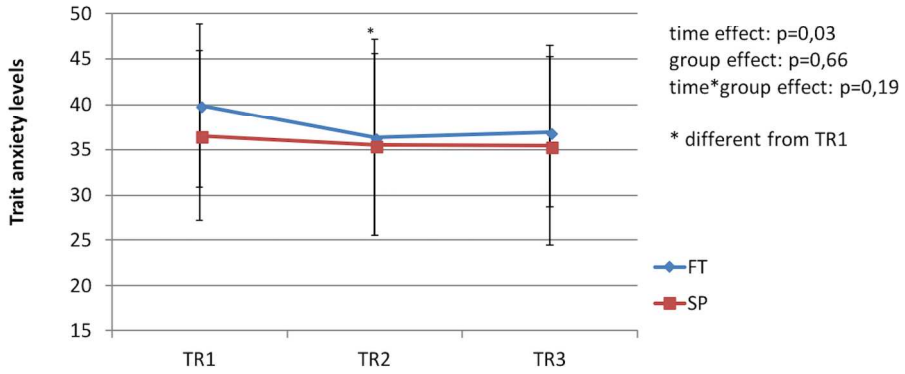

Evolution of trait anxiety in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

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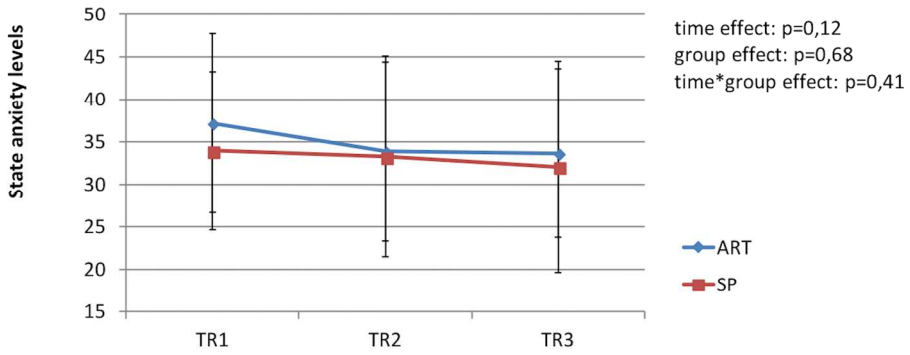

Evolution of state anxiety in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

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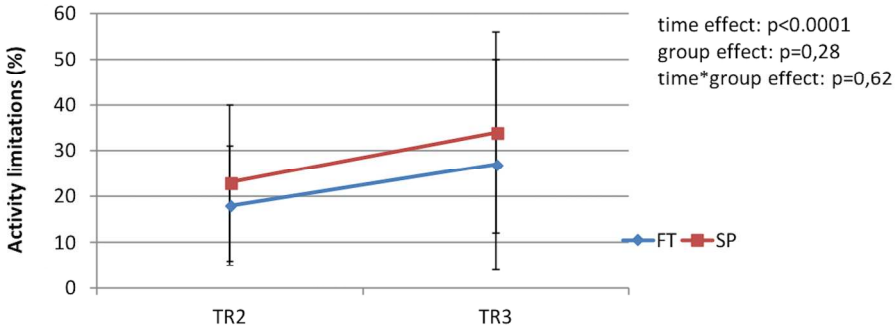

Evolution of activity limitations in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

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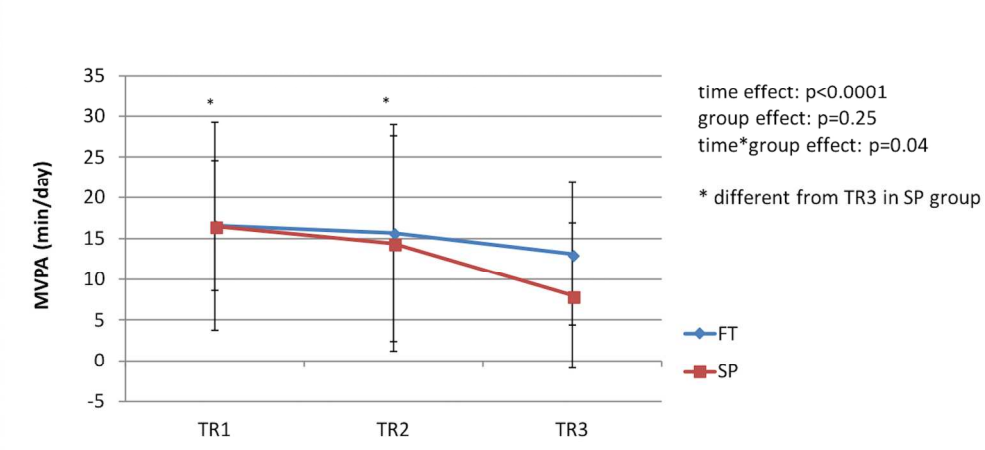

Evolution of daily moderate-to-vigorous physical activity (MVPA) in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

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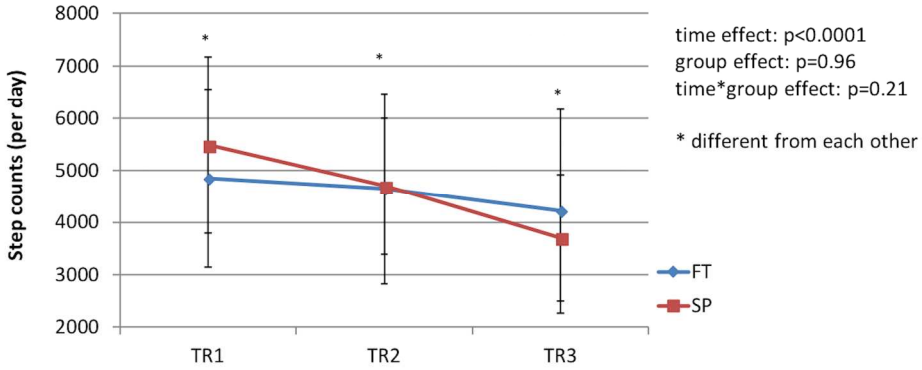

Evolution of daily step counts in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

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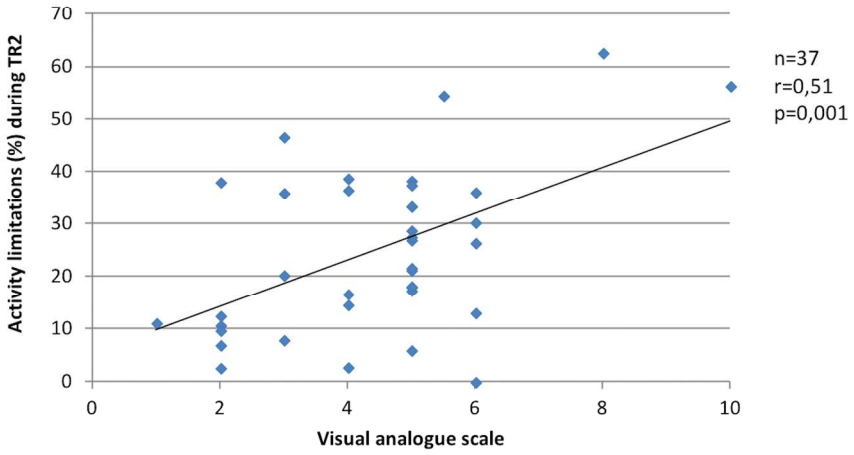

Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and activity limitations in the 2nd trimester of pregnancy (TR2).

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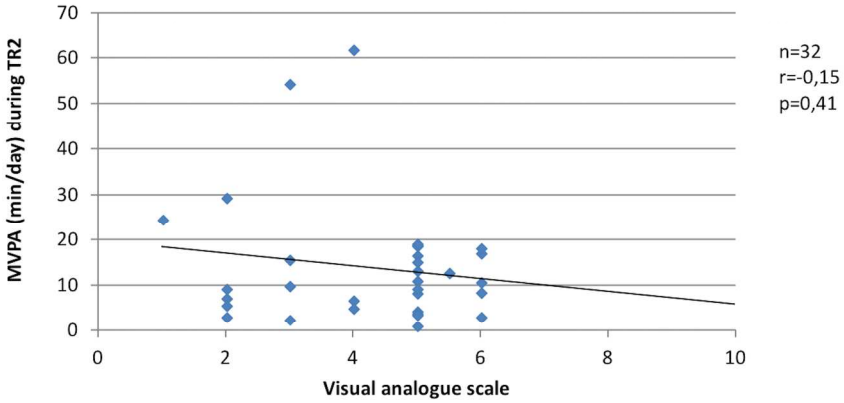

Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and daily moderate-to-vigorous physical activity (MVPA) in the 2nd trimester of pregnancy (TR2).

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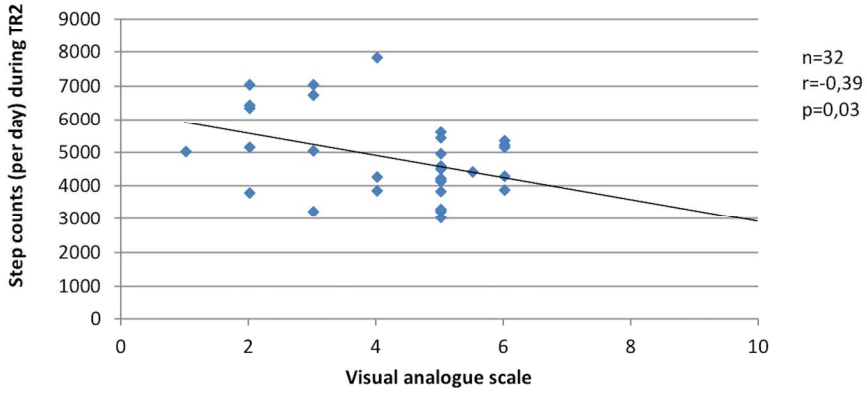

Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and daily step counts in the 2nd trimester of pregnancy (TR2).

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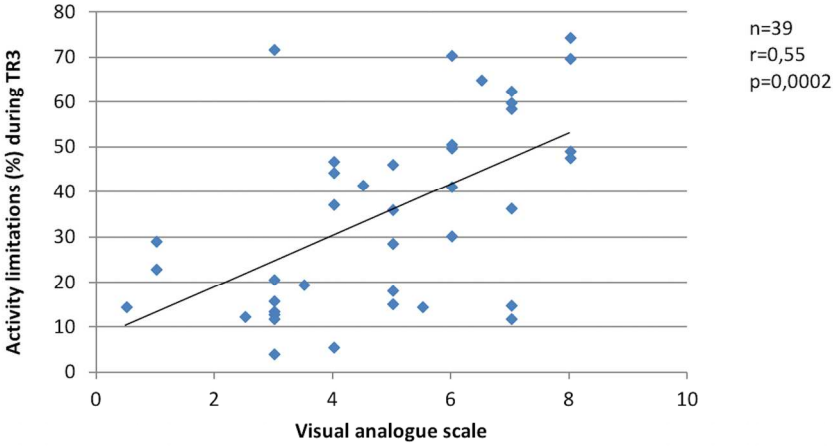

Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and activity limitations in the 3rd trimester of pregnancy (TR3).

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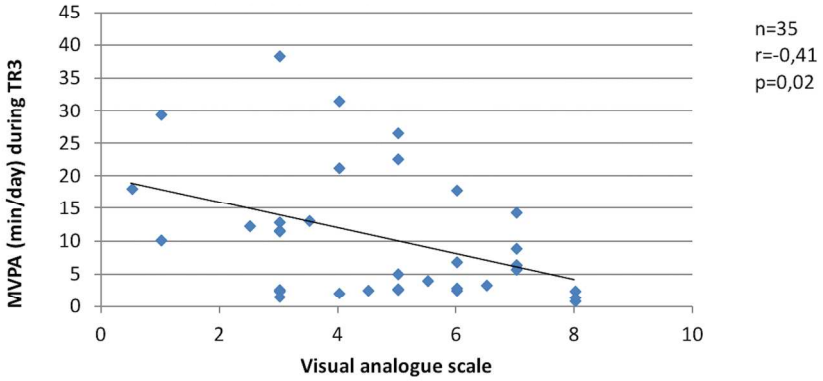
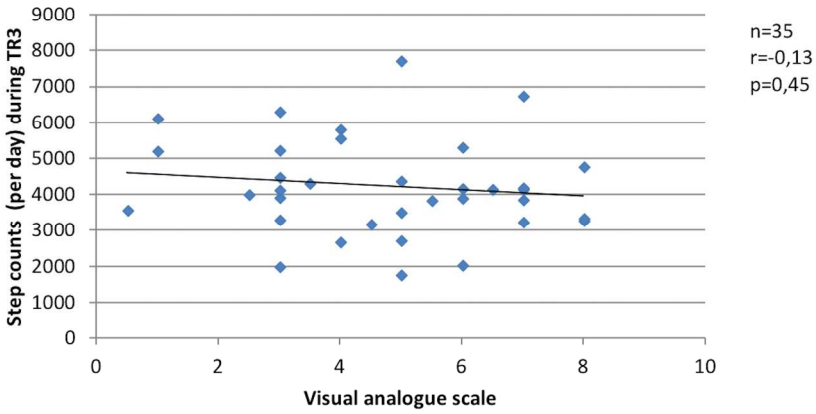


Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and daily moderate-to-vigorous physical activity (MVPA) in the 3rd trimester of pregnancy (TR3).

227x106mm (300 x 300 DPI)



Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and daily step counts in the 3rd trimester of pregnancy (TR3).

226x116mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	na
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	-
Study size	10	Explain how the study size was arrived at	-
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	na
		(*d*) If applicable, explain how loss to follow-up was addressed	na
		(*e*) Describe any sensitivity analyses	na
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8, 19 (table 1)
		(b) Indicate number of participants with missing data for each variable of interest	na
		(c) Summarise follow-up time (eg, average and total amount)	6
Outcome data	15*	Report numbers of outcome events or **summary measures over time**	8-9, 20-28 (figures)
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	na
		(*b*) Report category boundaries when continuous variables were categorized	na
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	na
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	na
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-11
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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

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Manuscript title: Lumbopelvic pain, anxiety, physical activity and mode of conception: A prospective cohort study of pregnant women

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ABSTRACT

Objectives: Pregnancy-related lumbopelvic pain (LPP) is a frequent condition known to significantly affect women's daily life. The etiology of pregnancy-related LPP pain is still not clearly established but the mode of conception has been suggested to contribute LPP. Anxiety related to fertility treatments may be one of the contributing factors. The primary objectives were to determine the evolution of LPP prevalence and severity, and anxiety, throughout pregnancy in women who conceived spontaneously (SP) or after fertility treatments (FT). A further aim was to examine the relationship between pregnancy-related LPP severity and anxiety. The secondary objective was to determine the evolution of physical activity and their correlation with the severity of pregnancy-related LPP.

Design: Prospective cohort study.

Setting: Pregnant women were recruited through physicians' referrals, posters and newspaper advertisements in the local and surrounding communities (hospital, maternity care clinic, prenatal centers, sports centers, local university) in the city of Trois-Rivières, Canada.

Participants: Fifty-nine pregnant women (33 SP and 26 FT) were assessed during the 1st, 2nd and 3rd trimester of pregnancy.

Primary and secondary outcome measures: Pregnancy-related LPP prevalence and severity (primary), trait and state anxiety, and physical activity levels (secondary).

Results: There was no relationship between the mode of conception and the outcome measures. The prevalence and severity of LPP increased over the course of pregnancy (time effect, $p<0.0001$) whereas trait anxiety decreased from early to mid-pregnancy (time effect, $p=0.03$). Activity limitations increased throughout pregnancy (time effect, $p<0.0001$) and physical activity levels decreased (time effect, $p<0.0001$). The severity of LPP was positively correlated with activity limitations ($r=0.51$ to 0.55) but negatively with physical activity levels ($r= -0.39$ to -0.41).

Conclusions: Maternal health-related factors, such as LPP, anxiety and physical activity, are not different in women who conceived spontaneously or after fertility treatments. The more LPP was severe, the more the women were physically limited and inactive.

Strengths and limitations of this study

- This is a prospective cohort study of pregnant women who were assessed at each trimester of pregnancy, allowing to determine the evolution of several maternal health-related factors that are known to change over the course of pregnancy;
- Primary and secondary outcomes were collected using validated tools;
- The low number of women who achieved a pregnancy following *in vitro* fertilization prevented us to fully test our hypotheses; thus larger studies are needed to better understand whether IVF contribute to pregnancy-related LPP.
- More than half of the participants had a university degree, which is not representative of our local population. The results may therefore not be broadly generalizable.

INTRODUCTION

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 the different periods during pregnancy LPP was assessed. The onset of LPP varies considerably, between the end of the first trimester to the first month post-delivery, with a peak of symptoms generally occurring between the 24th and 36th weeks of pregnancy [6]. 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]. 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].

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]. Another factor of interest is the mode of conception, in other words, naturally or after fertility treatments. A study reported that pregnant women who underwent *in vitro* fertilization (IVF) treatments had a two times higher prevalence rate of sacral pain in early

and late pregnancy, as well as a higher frequency of positive results on pelvic pain provocation tests in late pregnancy [15]. The authors concluded that relaxin causes pelvic pain because relaxin is higher in IVF pregnancies [16]. 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. As reported by a systematic review, women who conceived following fertility treatments had greater pregnancy-specific anxiety than those who conceived naturally[17]. Based on a multi-center study including 1,158 women, higher levels of anxiety was reported to be among the most notable factors associated with a higher likelihood of reporting LBP [18]. However, to the best of our knowledge, no study has examined pregnancy-related LPP among women who achieve pregnancy naturally or after fertility treatment, and whether anxiety is a contributing factor to the development of LPP.

The primary objectives of this prospective cohort study were to determine the evolution of LPP prevalence and severity, as well as anxiety, over the course of pregnancy in women who conceived naturally or after fertility treatments, and to examine the possible relationship between pregnancy-related LPP severity and anxiety levels. As pregnancy-related LPP has a significant impact on the women's daily life, the secondary objective of our study was to determine the evolution of physical activity behaviors throughout pregnancy and whether the severity of LPP was correlated to these factors. Our primary hypotheses are that LPP prevalence and severity, as well as anxiety levels will increase over the course of pregnancy but more strongly in women who conceived after fertility treatments, and that pregnancy-related LPP severity will be positively correlated with anxiety levels. As a result, our secondary hypotheses are that activity limitations will increase whereas physical activity behaviors will decrease over the course of pregnancy but more significantly in women who

conceived after fertility treatments, and that the severity of pregnancy-related LPP will be positively correlated with activity limitations but negatively with physical activity behaviors.

MATERIALS AND METHODS

Study design and participants' selection

This is a prospective cohort study of pregnant women who were recruited between October 2015 and September 2016. 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) in the city of Trois-Rivières, Canada. Women under 14 weeks of gestation, with a singleton pregnancy and able to understand, speak and write French were considered eligible to participate in the study. The study was approved by the local Research Ethics Committees (CER-2015-003 and CER-15-214-07.10) and all participants provided their written informed consent.

Outcome measures and measurement tools

Women were followed from the 1st trimester of pregnancy until delivery through three evaluations (1st trimester [TR1]: 10–16 weeks, 2nd trimester [TR2]: 24–28 weeks and 3rd trimester [TR3]: 32–36 weeks of gestation). 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]. If a woman had or was having pregnancy-related LPP, she was asked to rate pain intensity using a visual analog pain scale (VAS). This scale is a self-reported measurement tool used by health professionals allowing the patient to rate pain from 0 (no pain) to 10 (extreme pain) [20].

The levels of anxiety was assessed during TR1, TR2 and TR3 using the French-Canadian version [21] of the State-Trait Anxiety Inventory (STAI) [22]. The STAI is a self-reported questionnaire assessing the presence and severity of current symptoms of anxiety (state anxiety scale) and a generalized propensity to be anxious (trait anxiety scale). Each scale comprises 20 items rated with a 4-level Likert scale. The range of score for each scale is 20-80, the higher score indicating greater anxiety levels. 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].

Activity limitations and symptoms associated with pregnancy-related LPP were assessed in TR2 and TR3 using the completed the French-Canadian version of the PGQ was used [19]. The PGQ is a condition-specific measure developed for pregnant and postpartum women. It consists of 20 activity items and five symptom items on a four-point response scale and assesses activity limitations and symptoms associated with pain in the lumbopelvic region. The range of score is 0-100%, with a higher score indicating greater activity limitations and symptoms. The PGQ is reliable and valid for both pregnant and postpartum women with pregnancy-related LPP [24].

Finally, physical activity levels were objectively measured at each trimester of pregnancy using the ActiGraph GT3X (ActiGraph, Pensacola, FL), a triaxial accelerometer measuring data in a 60-s epoch. The women were instructed to wear the monitor over the hip on an elastic belt for seven consecutive days from wake-up time to bedtime. They were allowed to remove the accelerometer when sleeping, showering or engaging in water activities. Furthermore, the women received a daily diary to document wear and non-wear time periods and water activities. According to the method used in the Canadian Health Measures Survey, valid data were defined as four days or more of monitoring for 10 hours or more of wear time per day [25]. Pregnant women were encouraged to maintain their usual activities. Data were

processed using the Actilife software version 6.13.2 (ActiGraph, LLC, FL, USA). The accelerometer data obtained were averaged across valid wear days. To derive the activity frequency, intensity and duration of the measured activity in counts per minute per day, the Freedson equation was used: sedentary (<100 counts), light (100–1951 counts), moderate (1952–5724), vigorous (5725–9498), and very vigorous (>9498) [26], as previously used in pregnant women [27]. Non-wear time was defined as a period of zero counts for ≥ 60 consecutive minutes, admitting a maximum of two consecutive minutes between 1 and 100 counts/min. When a third observation was between 1 and 100 counts or one observation was more than 100 counts, the non-wear period was ended. Bouts of moderate-to-vigorous physical activity (MVPA) was defined as a minimum of 10 consecutive minutes above 1952 counts and ended with more than two consecutive records below this threshold.

Patient and Public Involvement

Patients and public were not involved in the design and conduct of this study. The results will not be disseminated to study participants.

Statistical analysis

Means and standard deviations, as well as percentages, were computerized for variables of interest. Student t-test was used to compare socio-demographic and anthropometric characteristics between SP and FT women. For categorical variables, the χ square test was used. 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]). 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 a significant effect of time, group or interaction effect

was found, post-hoc analyses were conducted using the Tukey test. To test whether the severity of pregnancy-related LPP was correlated to the levels of anxiety (objective 1), and physical activity behaviors (objective 2) at each trimester of pregnancy, Pearson's correlation analyses were used. Statistical analyses were performed by using the SAS software (Institute, Cary, NC, version 9.4) and the level of significance was set to *p-value* ≤ 0.05.

RESULTS

Between October 2015 and September 2016, the study was presented by physicians to 117 eligible pregnant women, among which 62 women accepted to participate. Reasons for not agreeing to participate to the study were lack of interest or lack of time. Three women (1 in SP group and 2 in FT group) were excluded due to loss to follow-up (n=1), miscarriage (n=1) or missing data (n=1), leaving 59 women (33 SP and 26 FT) for the statistical analyses.

The characteristics of pregnant women are presented in **Table 1**. No significant difference in socio-demographic and pre-pregnancy anthropometric characteristics was found between the groups ($p>0.05$). Women were on average in their early thirties and approximately half of them were nulliparous. More than half were of normal weight pre-pregnancy (BMI 18.5-24.9 kg/m^2) and had a university degree. Women's LPP history, related or not to a previous pregnancy, was also similar between the groups, with approximately 50% of the women reporting a history of LPP (**Table 1**). Finally, the prevalence and severity of pregnancy-related LPP, anxiety and physical activity levels were not different between SP and FT pregnant women at study entry (**Table 1**). Data showed that on average, women considered LPP as moderate (4/10) and were slightly anxious (35/80). Moreover, based on daily steps and physical activity recommendations [28 29], our population was considered inactive.

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. Furthermore, physical activity data was missing for 10 (17%), 7 (12%) and 8 (14%) women at TR1, TR2 and TR3, respectively, because those women did not wear the accelerometer for at least 10 hours per day for at least four days.

The prevalence of pregnancy-related LPP was similar in both groups during each trimester of pregnancy (TR1: $\chi^2 = 2.19$, p=0.33; TR2: $\chi^2 = 2.13$, p=0.33; TR3: $\chi^2 = 0.01$, p=0.92); the pooled prevalence increased from 42% during TR1 to 65% during TR2 to 68% during TR3 ($\chi^2 = 8.45$; p=0.01) (**Fig 1**). Among women presenting with pregnancy-related LPP at one time point during pregnancy (n=44, 26 SP and 18 FT), pain severity significantly increased over the course of pregnancy in both groups (time effect: F=14.81, p<0.0001. **Fig 2**), with pain severity being significantly higher during TR2 and TR3 compared to TR1. Trait anxiety decreased over the course of pregnancy in both groups (time effect: F=3.93, p<0.03. **Fig 3**), with lower levels during TR2 compared to TR1, whereas state anxiety did not significantly change (**Fig 4**). Finally, activity limitations associated with pregnancy-related LPP increased (time effect: F=18.82, p<0.0001. **Fig 5**) whereas daily steps decreased over the course of pregnancy in both groups (time effect: F=16.03, p<0.0001. **Fig 6).** The only time by group interaction effect was found for daily MVPA (time effect: F=13.11, p<0.0001; time*group interaction effect: F=3.38, p=0.04. **Fig 7),** with daily MVPA being lower in TR3 compared to TR1 and TR2 only in SP women.

Since changes in the severity of pregnancy-related LPP, levels of anxiety, and physical activity behaviors were similar between the groups, result from SP and FT women were pooled in the correlation analyses. Among women who presented with pregnancy-related LPP, no correlation was found during TR1 between the severity of pregnancy-related LPP and anxiety or physical activity levels. During TR2, the severity of pregnancy-related LPP was positively correlated with activity limitations (r=0.51, p=0.001, **Fig 8**) but negatively

with daily steps (r=-0.39, p=0.03, **Fig 9).** No correlation was found with daily MVPA **(Fig 10).** During TR3, we found a positive correlation between the severity of pregnancy-related LPP and activity limitations (r=0.55, p=0.0002, **Fig 11**) and a negative correlation with daily MVPA (r=-0.41, p=0.02, **Fig 12**). No correlation was found with daily steps **(Fig 13).**

DISCUSSION

To the best of our knowledge, this is the first cohort study assessing the course of pregnancy-related LPP prevalence and severity in pregnant women who conceived naturally and after fertility treatments, and possible association with anxiety levels and physical activity behaviors. Overall, our primary results showed no differences in LPP prevalence and severity, or anxiety levels between women who achieved a pregnancy naturally or after fertility treatments. 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]. Anxiety levels decreased from early to mid-pregnancy and were not correlated to the severity of LPP.

Only one study examined the evolution of the prevalence and severity of pregnancy-related PGP (PPGP) according to the mode of conception [15]. This study was conducted in 31 women who conceived after IVF and 200 women who conceived spontaneously and assessed PGP at 12, 24 and 34 weeks of pregnancy. The authors found an increase in PPGP prevalence and severity over the course of pregnancy in all women, as we and other authors did [30]. However, they reported a two times higher rate of PPGP in early and late pregnancy in women who achieved a pregnancy after IVF compared to those who achieved a pregnancy naturally but similar severity of PPGP [15]. 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.

Our hypothesis was that higher anxiety levels reported in women who conceived after fertility treatments [17] would contribute to higher pregnancy-related LPP prevalence and severity in this population of pregnant women. However, we did not find any difference in anxiety levels between women who conceived after fertility treatments and those who conceived naturally. Several reasons may explain our result. First, the majority of women included in our sample conceived after ovarian stimulation (OS, n=7) or intrauterine insemination (IUI, n=12), whereas the majority of studies included in Gourounti's review reporting higher anxiety in women who conceived following fertility treatments were conducted in the context of IVF [17]. 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.

When examining anxiety levels over the course of pregnancy, we found a U-shaped curve, with a significant decrease in anxiety from TR1 to TR2 and a non-significant trend toward an increase from TR2 to TR3. These findings are similar to those of previous studies [31 32]. In contrast, whereas some studies reported higher anxiety in pregnant women with LBP or PGP [18 33], we found no correlation between anxiety levels and LPP severity. Our findings suggest that in our sample, anxiety and LPP were two independent phenomena.

Likewise, our secondary results showed no relationship between the mode of conception and physical limitations and physical activity behaviors, except for MVPA during TR3. The decrease in MVPA observed only in women who conceived naturally needs further investigation. Similarly to previous studies [34-37], we found that with advancing pregnancy, physical limitations increased [36-38] and physical activity behaviors decreased [34 35 39]. Our data further showed that the greater pregnancy-related LPP severity the greater physical limitation and lower physical activity levels in mid- and late pregnancy. These results are also in

accordance with previous studies reporting decreased physical activity levels as physical limitations and low back pain increase with advancing pregnancy [36 40].

Limitations

The strength of our study is its longitudinal design that allowed us to examine the evolution of several maternal health-related factors that are known to change over the course of pregnancy, in the context of spontaneous pregnancies and pregnancies achieved following FT. Moreover, our study adds knowledge about the relationship between pregnancy-related LPP severity and physical activity behaviors. However, the current study has limitations that should be acknowledged. First, our sample was heterogeneous with regards to fertility treatments used to achieve a pregnancy, with the majority of women having conceived after OS or IUI. This may explain the lower prevalence of PPGP and anxiety levels in women who conceived after fertility treatments. 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. Second, more than half of the women we recruited had a university degree, which is more than in our local population (22.5%) [41]. This suggests a possible recruitment bias and limits the generalizability of our results. 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. We also had missing physical activity data because some women did not wear the accelerometer for at least 10 hours per day for at least four days. 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 do not 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.

CONCLUSION

In conclusion, our findings suggest that maternal health-related factors, such as LPP, anxiety and physical activity behaviors, are not different in women who conceived after fertility treatments and those who conceived spontaneously. The lack of correlation between the severity of pregnancy-related LPP and anxiety levels suggests that they are two independent phenomena. The increase in LPP severity and activity limitations, and decrease in physical activity behaviors with advancing gestation, and the fact that the more severe LPP the greater activity limitations and physical inactivity in mid- and late pregnancy underline the importance of pregnancy-related LPP management to allow pregnant women performing their daily activities.

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Declaration of conflicting interests: The authors declare that there is no conflict of interest.

Author Contributions: SMR, MD, VB contributed to the study concept and design; EL and AStL acquired the data; SMR, MD, EL performed the statistical analysis and interpreted the data; EL and SMR drafted the manuscript; MD, AStL and VB critically reviewed the manuscript for important intellectual content. All authors read and approved the final manuscript.

Competing interests: None declared.

Ethics approval: The study was approved by the local Research Ethics Committees (CER-2015-003 and CER-15-214-07.10)

Data sharing statement: No additional data are available.

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Table 1: Baseline characteristics of the 59 pregnant women included in study.

Variables	FT (n=26) Means ±SD	SP (n=33) Means ±SD	P values
Fertility treatments	OS=7 IUI=12 IVF=7	-	
Age (years)	32.2 ±3.6	30.9 ± 4.2	0.23
Parity	0.4 ± 0.6	0.6 ± 0.6	0.36
0 (n)	57.7% (15)	45.5% (15)	0.35
≥1 (n)	42.3% (11)	54.6% (18)	
Pre-pregnancy BMI (kg/cm^2)	26.3± 7.3	25.2 ± 6.6	0.54
Underweight <18.4	0% (0)	3.1% (1)	0.81
Normal weight (18.5-24.9)	60.0 (15)	62.5% (20)	
Overweight (25.0-29.9)	20.0 (5)	18.8% (6)	
Obese ≥30.0	20.0%(5)	15.6% (5)	
Education levels			
Non-university degree	42.3% (11)	33.3% (11)	0.48
University degree	57.7% (15)	66.7% (22)	
LPP history (yes) [1]	46.2% (12)	54.6% (18)	0.52
Prevalence of pregnancy-related LPP over the last week (yes)	34.6% (9)	48.5% (16)	0.33
Severity of pregnancy-related LPP over the last week	2.9 ± 1.9	4.1± 2.3	0.18
State anxiety	37.4 ± 11.6	34.2 ± 9.1	0.28
Trait anxiety	39.8 ± 10.0	37.1 ± 9.4	0.26
Daily steps	5328 ± 1551	5569 ± 1552	0.80
Daily MVPA (min)	16.3 ± 10.0	17.4 ± 13.2	0.97

FT: fertility treatment; SP: spontaneous conception; OS: ovarian stimulation; IUI: intrauterine insemination; IVF: *in vitro* fertilization; BMI : body mass index; LPP : lumbopelvic pain; MVPA: moderate-to-vigorous physical activity

[1] LPP history includes history of pregnancy-related LPP and LPP not related to pregnancy

Missing data: pre-pregnancy BMI: 1 FT, 1 SP; state and trait anxiety : 1 SP; accelerometer data: 4 SP; 6 FT

Figure legend

Figure 1: Prevalence of pregnancy-related lumbopelvic pain (LPP) in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

Figure 1 footnote: TR1: 1st trimester of pregnancy; TR2: 2nd trimester of pregnancy; TR3: 3rd trimester of pregnancy.

Figure 2: Evolution of pregnancy-related lumbopelvic pain (LPP) severity in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

Figure 2 footnote: TR1: 1st trimester of pregnancy; TR2: 2nd trimester of pregnancy; TR3: 3rd trimester of pregnancy.

Figure 3: Evolution of trait anxiety in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

Figure 3 footnote: TR1: 1st trimester of pregnancy; TR2: 2nd trimester of pregnancy; TR3: 3rd trimester of pregnancy.

Figure 4: Evolution of state anxiety in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

Figure 4 footnote: TR1: 1st trimester of pregnancy; TR2: 2nd trimester of pregnancy; TR3: 3rd trimester of pregnancy.

Figure 5: Evolution of activity limitations in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

Figure 5 footnote: TR1: 1st trimester of pregnancy; TR2: 2nd trimester of pregnancy; TR3: 3rd trimester of pregnancy.

Figure 6: Evolution of daily moderate-to-vigorous physical activity (MVPA) in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

Figure 6 footnote: TR1: 1st trimester of pregnancy; TR2: 2nd trimester of pregnancy; TR3: 3rd trimester of pregnancy.

Figure 7: Evolution of daily step counts in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

Figure 7 footnote: TR1: 1st trimester of pregnancy; TR2: 2nd trimester of pregnancy; TR3: 3rd trimester of pregnancy.

Figure 8: Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and activity limitations in the 2nd trimester of pregnancy (TR2).

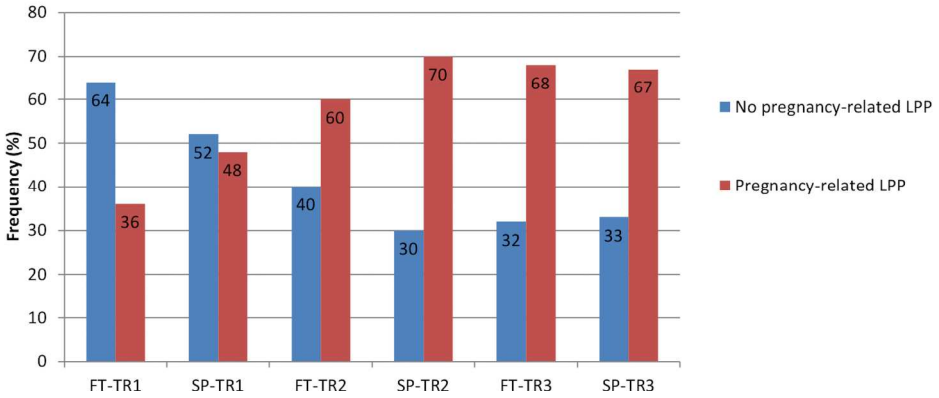
Figure 9: Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and daily moderate-to-vigorous physical activity (MVPA) in the 2nd trimester of pregnancy (TR2).

Figure 10: Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and daily step counts in the 2nd trimester of pregnancy (TR2).

Figure 11: Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and activity limitations in the 3rd trimester of pregnancy (TR3).

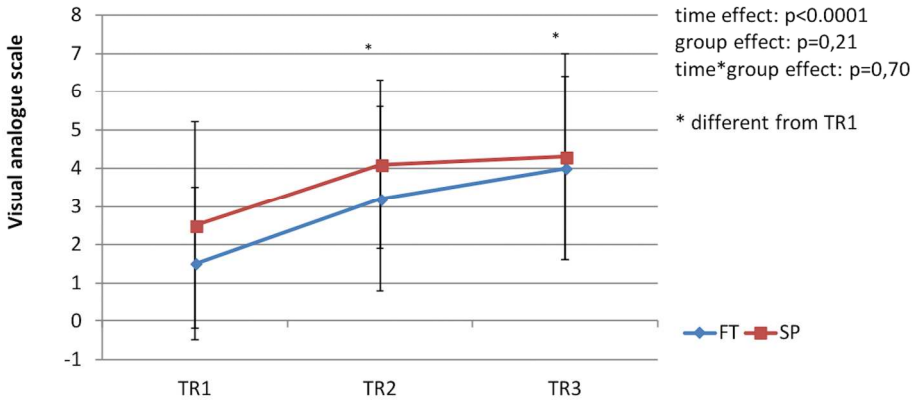
Figure 12: Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and daily moderate-to-vigorous physical activity (MVPA) in the 3rd trimester of pregnancy (TR3).

Figure 13: Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and daily step counts in the 3rd trimester of pregnancy (TR3).



Prevalence of pregnancy-related lumbopelvic pain (LPP) in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

263x132mm (300 x 300 DPI)



Evolution of pregnancy-related lumbopelvic pain (LPP) severity in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

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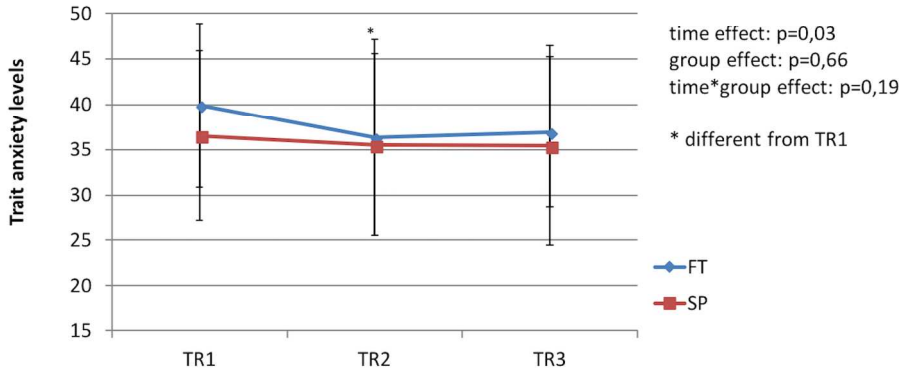

Evolution of trait anxiety in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

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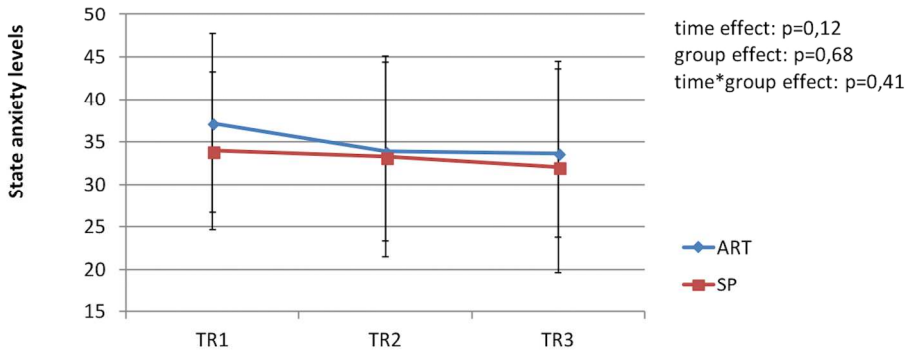

Evolution of state anxiety in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

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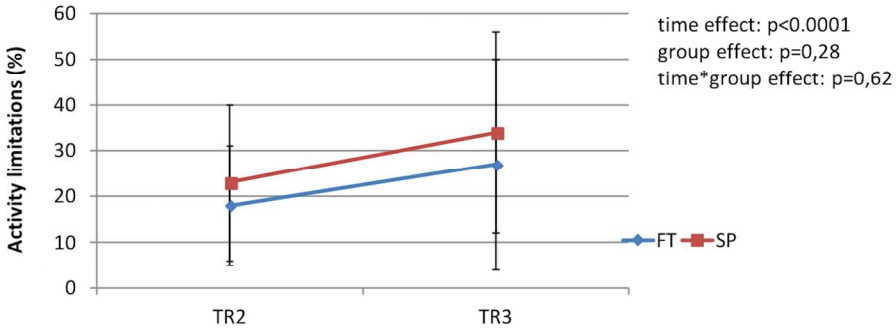

Evolution of activity limitations in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

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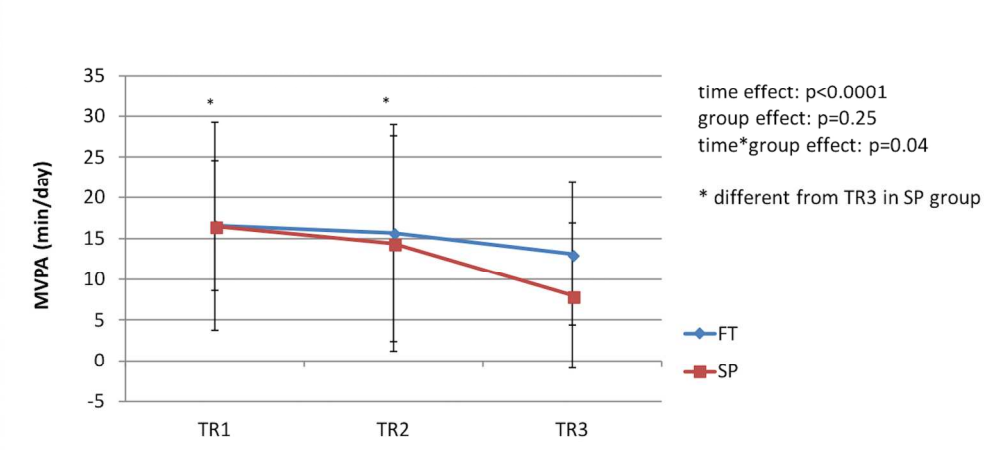

Evolution of daily moderate-to-vigorous physical activity (MVPA) in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

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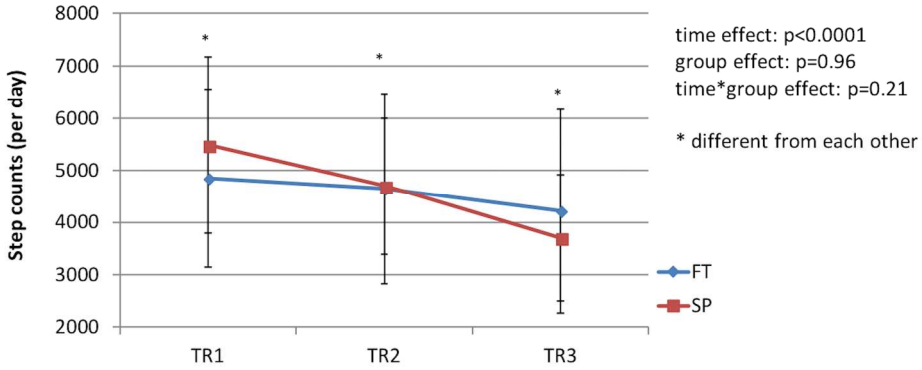
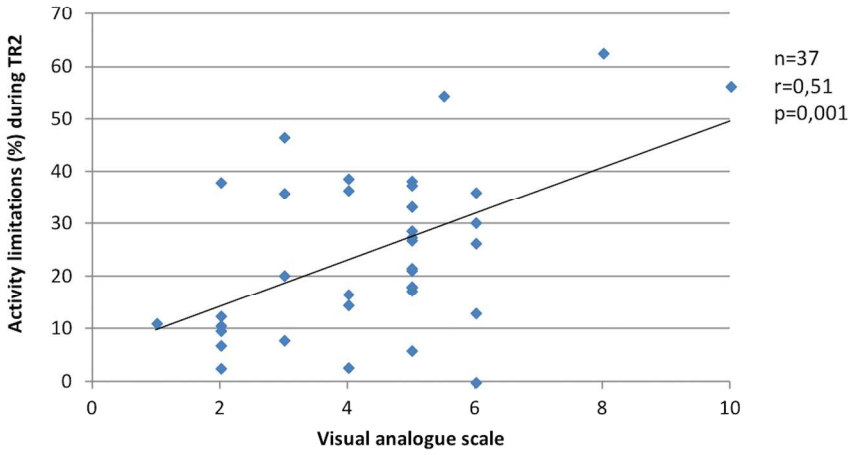


Evolution of daily step counts in women who conceived spontaneously (SP) or after fertility treatments (FT) over the course of pregnancy.

225x106mm (300 x 300 DPI)



Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and activity limitations in the 2nd trimester of pregnancy (TR2).

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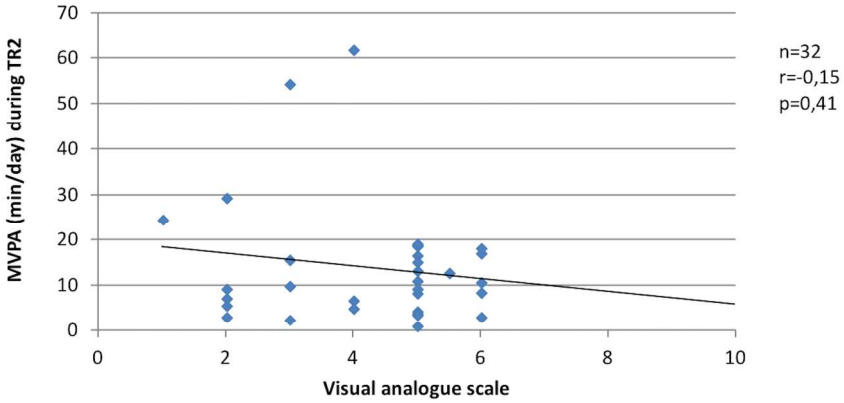

Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and daily moderate-to-vigorous physical activity (MVPA) in the 2nd trimester of pregnancy (TR2).

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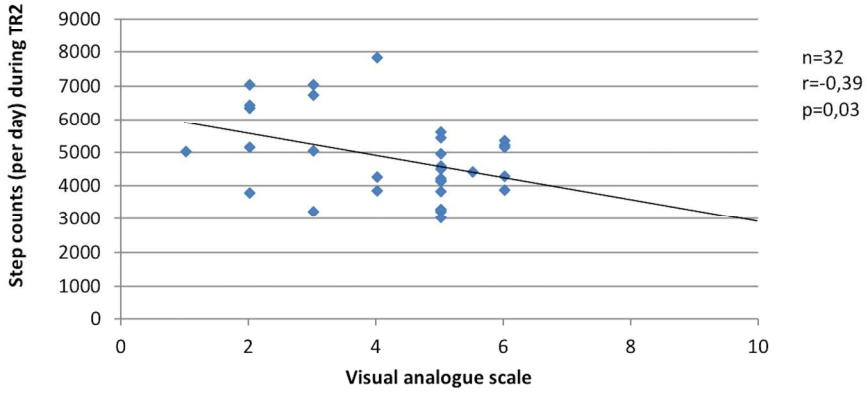
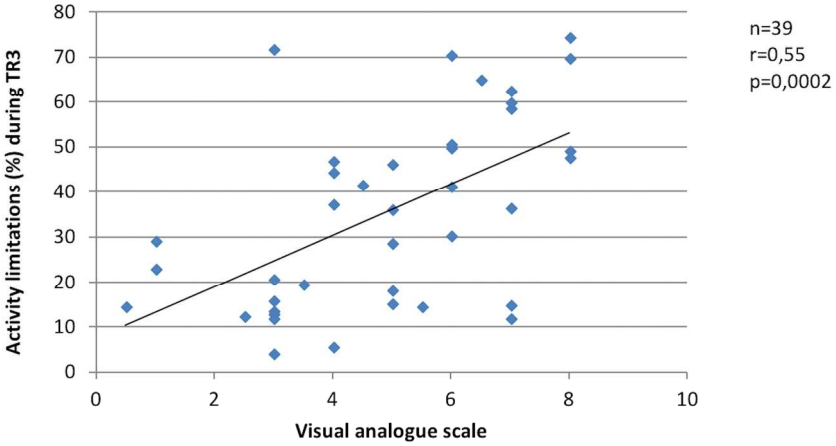


Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and daily step counts in the 2nd trimester of pregnancy (TR2).

234x109mm (300 x 300 DPI)



Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and activity limitations in the 3rd trimester of pregnancy (TR3).

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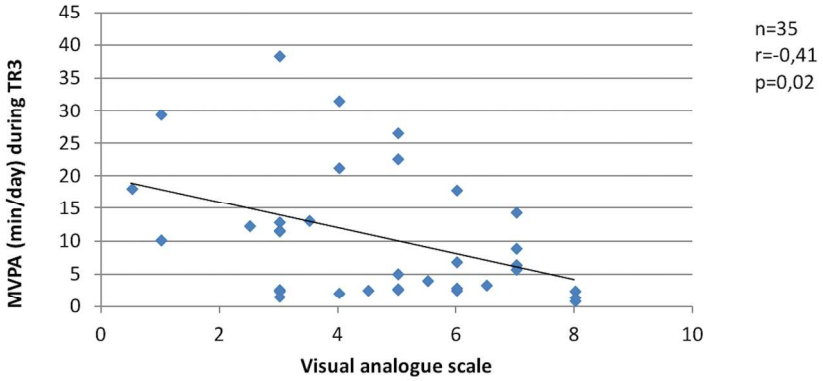
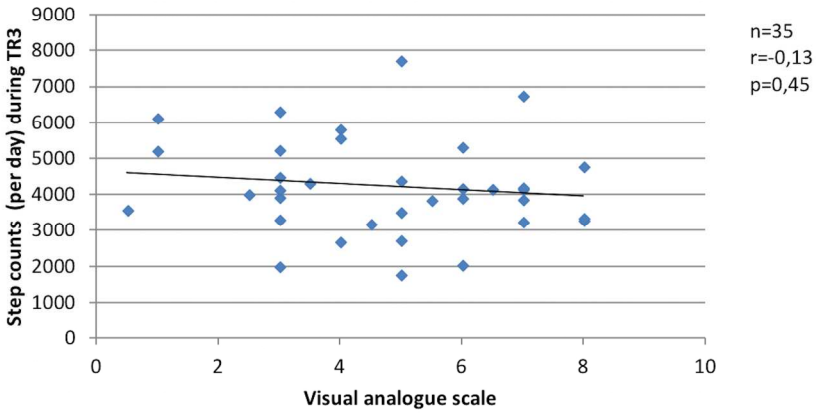


Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and daily moderate-to-vigorous physical activity (MVPA) in the 3rd trimester of pregnancy (TR3).

227x106mm (300 x 300 DPI)



Correlation between the severity of pregnancy-related lumbopelvic pain (LPP) and daily step counts in the 3rd trimester of pregnancy (TR3).

226x116mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	na
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	-
Study size	10	Explain how the study size was arrived at	-
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	na
		(*d*) If applicable, explain how loss to follow-up was addressed	na
		(*e*) Describe any sensitivity analyses	na
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8, 19 (table 1)
		(b) Indicate number of participants with missing data for each variable of interest	na
		(c) Summarise follow-up time (eg, average and total amount)	6
Outcome data	15*	Report numbers of outcome events or **summary measures over time**	8-9, 20-28 (figures)
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	na
		(*b*) Report category boundaries when continuous variables were categorized	na
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	na
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	na
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-11
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.