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Adverse events from spinal manipulations in the pregnant and postpartum periods: a systematic review and update

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Background: *The purpose of this study is to update a previous critical review of adverse events in pregnant and postpartum populations.*

Methods: *The following databases were searched: PubMed, CINAHL, Index to Chiropractic Literature, Cochrane Database of Systematic Reviews/Cochrane Central Register of Controlled Trials and MEDLINE. We included all study design types as it was determined a priori that there would not be enough high-quality research on spinal manipulative therapy (SMT) in these populations to make any determinations. The Scottish Intercollegiate Guidelines Network (SIGN) and CARE (CAse REport) checklists were used for quality rating.*

Results: *This update found one case study that demonstrated a serious adverse event in the cervical*

Manipulations vertébrales chez la femme enceinte et la femme en postpartum : mise à jour : mise à jour d'une étude sur les effets indésirables

Contexte : *La présente étude vise à mettre à jour les résultats d'un examen critique des effets défavorables des manipulations vertébrales chez la femme enceinte et la femme en postpartum.*

Méthodologie : *On a interrogé les bases de données suivantes : PubMed, CINAHL, Index to Chiropractic Literature, Cochrane Database of Systematic Reviews/ Cochrane Central Register of Controlled Trials et MEDLINE. On a retenu toutes les études parce qu'il avait été établi antérieurement que le nombre de recherches de bonne qualité sur les manipulations vertébrales (MV) chez la femme enceinte et la femme en postpartum était insuffisant pour trancher toute question. On s'est servi des listes de vérification Scottish Intercollegiate Guidelines Network (SIGN) et CARE (CAse REport) pour évaluer la qualité des études.*

Résultats : *Une étude de cas faisait état d'un grave effet indésirable à la colonne cervicale après des*

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spine following SMT and a handful of minor and transient adverse events in the low back following SMT.

Conclusions: *There was limited evidence of adverse events following SMT in these populations. Although we are calling for improved reporting of such events in future studies, it may be that such injuries are rare.*

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KEY WORDS: chiropractic, spinal manipulative therapy, manual therapy, pregnancy, postpartum, adverse events

MV et d'une poignée d'effets indésirables mineurs et transitoires à la colonne lombaire.

Conclusions : *Il existe peu de preuves que les MV ont des effets indésirables chez les populations à l'étude. Il faudrait plus de données. Mais il est permis d'affirmer que ces effets indésirables sont rares.*

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MOTS CLÉS : chiropratique, manipulations vertébrales, grossesse, postpartum, effets indésirable

Introduction

Musculoskeletal pain is a frequent complaint during pregnancy and the postpartum period. Low back pain (LBP), pelvic girdle pain (PGP), carpal tunnel syndrome, and mid-back pain are common complaints in these groups, with LBP being the most common complaint among pregnant women. The prevalence of low back pain during pregnancy has been reported as up to 90% of pregnant women[1-6] and may continue into the postpartum period with up to 75% of women reporting symptoms six months following birth[7-12] and approximately 8-20% still suffering from pregnancy-related pain two to three years after giving birth[13]. Both pregnant and postpartum women have described the back pain as moderate, severe or disabling[1, 7] and interfering with life in general; interrupting activities of daily living, sleep and child rearing[1, 8, 13, 14]. Unfortunately, many primary health care providers consider pregnancy-related back pain to be a normal and unavoidable occurrence[15-17] and patients often receive little or no treatment suggestions to manage their condition[18,19].

The etiology of pregnancy-related back pain is unknown.[17, 20] It has been suggested that causation is multifactorial and some of the proposed mechanisms include, but are not limited to, maternal weight gain, biomechanical changes due to pregnancy[17, 21], changes in abdominal musculature to accommodate the growing fetus[22-24] and/or increased circulating relaxin[25] producing ligamentous laxity[26]. In general, women are more susceptible to increases in joint laxity than men.[27, 28] It has been suggested that hormonal changes may be responsible for these differences.[29-31] By the twelfth week of pregnancy production of the hormone relaxin is increased and "relaxes" the joints and ligaments for labour and delivery of the baby through the vaginal canal.[32,33] This change in hormonal milieu does not dissipate upon delivery and it is suggested that women immediately postpartum may continue to experience hormone-mediated ligament laxity. It is important to note that this increase in ligament laxity is not targeted just at the pelvis[34] thereby making these women more susceptible to various musculoskeletal injuries during this time.

Low back pain (LBP)[35], neck pain[36-38] and headaches[39] are significant causes of pain and disability in the non-pregnant population. Approximately 80% of the population experience at least one episode of LBP in their lifetime[35], 30-50% experience neck pain in a given year[40] and approximately 50% of people will experience a headache within the last year[41]. One effective treatment option for patients experiencing any of these pains includes spinal manipulative therapy (SMT)[42-47]; whereby a localized force of high velocity and low amplitude (HVLA) is applied in the direction of the spinal segment. In the non-pregnant population, severe adverse events following SMT are rare[48-53] with most events being reported in lower level of evidence studies such as case reports or case series[54, 55]. It is noteworthy that there are published case reports describing vertebral artery dissection and stroke following manipulation in the non-pregnant population.[52] However, most cases of extracranial vertebral artery dissections are thought to occur spontaneously in individuals with other risk factors such as connective tissue disorders, migraine, hypertension or vessel abnormalities.[52] At this

time, the current evidence does not find excess risk for vertebral artery dissection from individuals seeking care from chiropractors compared to primary care.[52, 56]

Effective treatment options for pregnancy or postpartum related-back pain are not well known.[57-59] There are few well designed randomized controlled trials[60-62] (RCTs) investigating chiropractic care on pregnancy and postpartum-related spine pain, with most of the current evidence for this population being case studies. Although chiropractors report seeing pregnant and postpartum patients regularly[59, 63], the lack of evidence for these two populations is surprising given the impact pain can have on a woman's life during these time periods. Similarly, there is little information regarding the safety of treatment options, such as SMT, in these populations. Given the coagulability status[64, 65] of these women and the plethora of hormonal and biomechanical changes that occur as a result of pregnancy and into the postpartum period, it is possible that some treatment options, such as SMT, may be contraindicated in these populations.

Our 2012 critical review of the literature identified four case reports[50, 51, 66, 67] and one prospective observational cohort study[68] reporting adverse events in seven individuals (five pregnant and two postpartum) following SMT[69]. Events ranged from minor pain following treatment, to fracture, stroke and epidural hematoma. This is an update of that previous paper and our aim is to systematically review the literature for any reported cases of iatrogenic injuries following SMT and other manual treatments.

Methods

Similar to our first review[69], in this updated review we determined *a priori* that limiting our review to systematic reviews (SR) and RCTs would exclude valuable information regarding adverse events, so cohort and case reports were included. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews (PRISMA) and was registered with PROSPERO (no. CRD42019048918).

Literature search parameters

A literature search strategy (Appendix 1) was developed in collaboration with a health sciences librarian (KM). The following items were considered in developing the strategy:

Participants/Population

Women who were either pregnant or postpartum (up to 6 weeks after birth) with spine and/or pelvic girdle musculoskeletal complaints.

Intervention

The interventions examined included spinal SMT and any other manual therapies performed by chiropractors, osteopaths and physiotherapists; as the latter two can deliver similar treatment plans to pregnant women, these terms were also included.[57, 58, 70]

Comparators

There were no restrictions for the comparison group which may include: active treatments (such as exercise), placebos/shams, usual obstetric care (UOBC) or no treatments.

Outcomes

The presence of adverse events/iatrogenic injuries.

Search strategy

The following databases were used in the search strategy: PubMed, CINAHL, Index to Chiropractic Literature, Cochrane Database of Systematic Reviews/Cochrane Central Register of Controlled Trials and MEDLINE. Search terms consisted of subject headings specific to each database (i.e. MeSH in MEDLINE) and free text words relevant to pregnancy, postpartum, low back pain, pelvic girdle pain, chiropractic, etc. Publications in the search were restricted to the English language and from the date of our last review (October 2011) until November 2018. An additional search strategy was employed when reviewing systematic reviews (SR). Similar to Hawk *et al*.[71] and others[46], two investigators (CAW and SW) searched each included SR for eligible studies not identified through the formal search. Any that were deemed potentially acceptable were added to the list of studies to be analyzed.

Screening

Titles were screened independently by two reviewers (SW and CAW). Disagreements on eligibility were resolved by discussion. The same two investigators reviewed the abstracts and articles. If there was disagreement between the reviewers, a third investigator also reviewed (KS) either

Inclusion	Exclusion
Studies that address adverse events including: Randomized control trials Cohort Studies Any other clinical trials Case studies Case reports	Studies that do not address adverse events Non-peer reviewed publications Commentaries/editorials/ letters No treatment outcomes Non-clinical studies A score of *"unacceptable"* by the SIGN criteria for SRs, RCTs and cohort studies

Figure 1.
Inclusion and exclusion criteria

the abstract or full-text article and the majority rating was used following a group discussion. Studies of unacceptable quality were excluded from the evidence tables.

Eligibility criteria

The eligibility criteria for articles in the search can be found in Figure 1.

Evaluation of risk of bias

As previously performed by Hawk *et al*.[71] and others[57, 58] the Scottish Intercollegiate Guideline Network (SIGN) checklists were used to evaluate systematic reviews/meta-analyses[72] (both abbreviated as "SR") and cohort studies[73] and a modified SIGN checklist was used to review

Item		Yes/No[a]
1.1	The research question is clearly defined, and the inclusion/exclusion criteria must be listed in the paper.	
1.2	A comprehensive literature search is carried out.	
1.3	At least 2 people should have selected studies.	
1.4	At least 2 people should have extracted data.	
1.5	The status of publication was not used as inclusion criteria.	
1.6	The excluded studies are listed.	
1.7	The relevant characteristics of the included studies are provided.	
1.8	The scientific quality of the included studies was assessed and reported.	
1.9	Was the scientific quality of the included studies used appropriately?	
1.10	Appropriate methods are used to combine the individual findings.	
1.11	The likelihood of publication bias was assessed appropriately.	
1.12	Conflict of interests are declared.	
	Total score[b]	

Figure 2.
SIGN checklist for systematic review[72]

SIGN – Scottish Intercollegiate Guideline Network
[a]Rating: "Yes" = 1, "No" or unable to tell from the article = 0
[b]Scoring: Sum of items - >9 high quality, low risk of bias; 6-9 acceptable quality, moderate risk of bias; <6 low quality, high risk of bias; if 1 and/or 3 are "no" Unacceptable quality (reject)

Item		Yes/No[a]
1.1	The study addresses an appropriate and clearly focused question.	
1.2	The assignment of subjects to treatment groups is randomized.	
1.3	An adequate concealment method is used.	
1.4	The design keeps subjects and investigators "blind" about treatment allocation.	
1.5	The treatment and control groups are similar at the start of the trial.	
1.6	The only difference between groups is the treatment under investigation.	
1.7	All relevant outcomes are measured in a standard, valid and reliable way.	
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	
1.9	All the subjects are analyzed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).	
1.10	Where the study is carried out at more than one site, the results are comparable for all sites.	
	Total score[b]	

Figure 3.
Modified SIGN Randomized controlled trial checklist[74]

SIGN – Scottish Intercollegiate Guideline Network
[a]Rating: "Yes" = 1, "No" or unable to tell from the article = 0
[b]Scoring: Sum of items - 9-10 high quality, low risk of bias; 6-8 acceptable quality, moderate risk of bias; 3-5 low quality, high risk of bias; 0-2 or if item 1 and/or 3 are "no" unacceptable quality (reject)

Item		Yes/No[a]
1.1	The study addresses appropriate and clearly focused question	
1.2	The two groups being studied are selected from source populations that are comparable other than the factor under investigation. Only when there is a comparison group.	
1.3	The study indicates how many of the people asked to take part did so, in each of the groups being studied. Only in prospective, multiple cohort studies.	
1.4	The likelihood that some eligible subjects might have outcome at the time of enrolment is assessed and taken into account in the analysis	
1.5	It was revealed what percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed. In prospective studies.	
1.6	A comparison is made between full participants and those lost to follow-up, by exposure status. Only in prospective, multiple cohort studies.	
1.7	The outcomes are clearly defined.	
1.8	The assessment of outcome is made blind to exposure status. In studies with more than one group.	
1.9	Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome.	
1.10	The measure of assessment of exposure is reliable	
1.11	Evidence from other sources is used to demonstrate that the method of outcome is valid and reliable. Whenever any kind of subjective measure is used.	
1.12	Exposure level or prognostic factor is assessed more than once. Prospective studies only.	
1.13	The main potential confounders are identified and taken into account adequately in the design and analysis.	
1.14	Confidence intervals are provided.	
	Total score[b]	

Figure 4.
SIGN Cohort study checklist[73]

SIGN – Scottish Intercollegiate Guideline Network
[a]Rating: "Yes" = 1, "No" or unable to tell from the article = 0
[b]Scoring: Sum of items – 12-14 high quality, low risk of bias; 9-11 acceptable, moderate risk of bias; 6-8 low quality, high risk of bias; <6 unacceptable quality.

RCTs[71, 74]. The modified SIGN RCT checklist combined information from the original checklist about concealment and blinding of the investigators, and it added three other items including patient blinding, sample size justification and if the required sample same size was reached (items 3, 4, 5 and 9). Unlike the original SIGN RCT checklist[74], the modified one did not take into consideration drop-outs or compare results from different sites[71]. Two of the original The SIGN checklists score each article as "*high quality, low risk of bias*", "*acceptable quality, moderate risk of bias*", "*low quality, high risk of bias*" or "*unacceptable*" quality. Any studies that were scored as "*unacceptable*" quality were removed from further analysis. Each level was defined by scoring the checklists and assigning a value of "1" for each "yes" response. Figures 2, 3 and 4 list the items in each checklist and explain the scoring system used to determine quality rating.

For case reports, the CARE (CAse REport) checklist for case reports was employed.[75] The CARE checklist evaluates 13 main areas over 30 specific items (Figure 5). Although there is no scoring system for this checklist, we decided *a priori* that each item would be worth "1" and a high score would indicate a more robust case report. A consensus-based decision between reviewers on whether the internal validity of the case reports was acceptable for inclusion in the current review.

Two investigators (CAW and SW) evaluated each article. If there was a disagreement between the two reviewers, a third investigator (KS) was asked to review. The majority rating was used after discussion among reviewers.

Data extraction

Variables for data extraction was determined *a priori* and completed by two investigators (CAW and SW) and the third author (KS) verified all of the data presented in the tables. All information extracted was entered into a Microsoft Word table.

Systematic Reviews (SRs)

Information extracted from SRs included: citation (first author and year of publication) and quality assessment, type of treatment/intervention, number of studies included, number of participants and type of studies included, results of that assessment and overall conclusions of the review.

Randomized Controlled Trials (RCTs)

Information extracted from RCTs included: study identification by citation (first author and year of publication) and quality assessment, patient population information, mean age and mean symptom duration, treatment/intervention, comparison group, dosage, adverse events reported and overall study conclusions.

Cohort studies

Information extracted from cohort studies included: study identification by citation (first author and year of publication) and quality assessment, patient population information, mean age and mean symptom duration, intervention, dosage, adverse events reported and overall study conclusions.

Case reports

Data extracted from the case reports included: study identification by citation (first author and year of publication), case presentation, treatment, and adverse events reported.

Item		**Description**	
1	Title	The area of focus and "case report" should appear in the title	
2	Key words	Two to five key words that identify topics in the case report	
3	Abstract	a.	Introduction – What is unique and why is it important?
		b.	The patient's main concerns and important critical findings
		c.	The main diagnoses, interventions and outcomes
		d.	Conclusion – What are one or more "takeaway" lessons
4	Introduction	Briefly summarize why this case is unique with medical literature references	
5	Patient Information	a.	De-identified demographic and other patient information
		b.	Main concerns and symptoms of the patient
		c.	Medical, family and psychosocial history including genetic information
		d.	Relevant past interventions and their outcomes
6	Clinical findings	Relevant physical examination (PE) and other clinical findings	
7	Timeline	Relevant data from this episode of care organized as a timeline (figure or table)	
8	Diagnostic Assessment	a.	Diagnostic methods (PE, laboratory testing, imaging, surveys)
		b.	Diagnostic challenges
		c.	Diagnostic reasoning including differential diagnosis
		d.	Prognostic characteristics when applicable
9	Therapeutic Interventions	a.	Types of intervention (pharmacological, surgical, preventative)
		b.	Administration of intervention (dosage, strength, duration)
		c.	Changes in the intervention with explanations
10	Follow-up and Outcomes	a.	Clinician and patient-assessed outcomes when appropriate.
		b.	Important follow-up diagnostic and other test results
		c.	Intervention adherence and tolerability (how this was assessed)
		d.	Adverse and unanticipated events
11	Discussion	a.	Strength and limitations in your approach to this case
		b.	Discussion of the relevant medical literature
		c.	The rationale for your conclusions
		d.	The primary "take-away" lessons from this case report
12	Patient perspective	The patient can share their perspective on their case	
13	Informed Consent	The patient should give informed consent	

Figure 5. *CAse REport (CARE) Checklist*[75]

Table 1.
Risk of bias assessment of included SRs with the SIGN checklist.

First author and year published	Items on SIGN checklist[a]													
	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	Total	Quality[b]
Liddle, 2015[76]	1	1	1	1	0	1	1	1	1	1	1	1	11	H
Franke, 2017[78]	1	1	1	1	0	1	1	1	1	1	1	1	11	H
Ruffini, 2013[77]	1	1	1	1	0	1	1	1	1	1	1	1	11	H
Hall, 2016[18]	1	1	1	1	1	1	1	1	1	1	1	1	12	H
Gutke, 2015[70]	1	1	0	1	0	1	1	1	1	0	1	1	9	A
Sharma, 2014[79]	1	1	1	1	0	0	1	1	1	1	0	0	8	A
Majchrzyki, 2015[80]	0	0	0	0	0	0	0	0	0	0	0	0	0	U
Posadaski, 2011[81]	0	0	0	0	0	0	0	0	0	0	0	0	0	U

SIGN = Scottish Intercollegiate Guideline Network
[a,b]See Figure 2 for Quality assessment SIGN checklist items[a] and scoring[b] for SRs

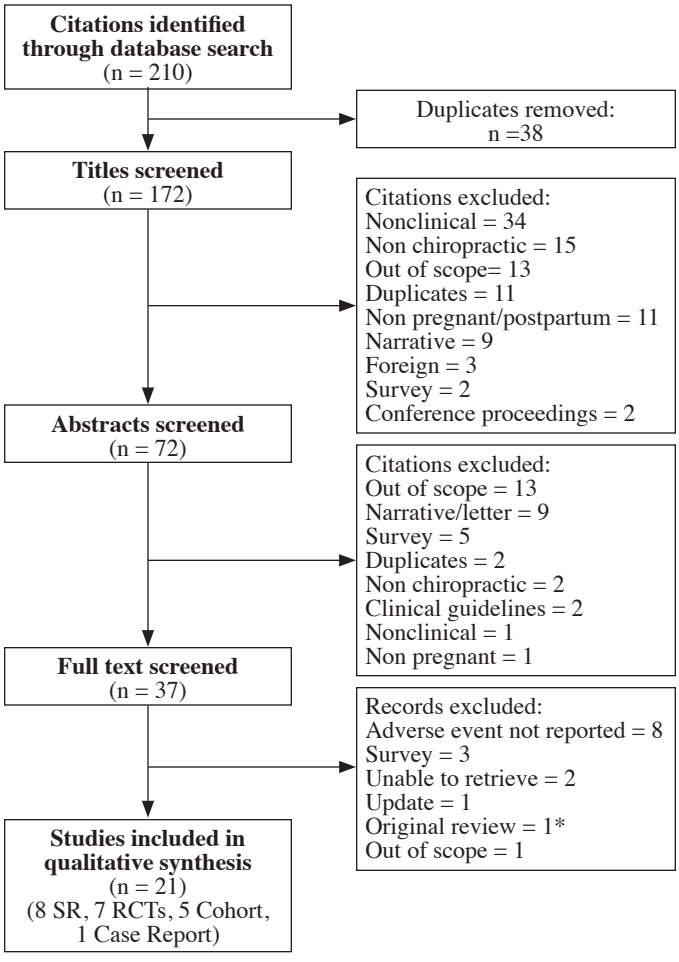

Figure 6.
Preferred reporting items for systematic reviews and meta-analysis (PRISMA) flow diagram.
*Stuber et al. (2012) not included in this analysis

Results

The initial database searches yielded 210 manuscripts (172 after duplicates removed). Of these, 21 were included in the review (8 SRs, 7 RCTs, 5 cohort, and 1 case study); see Figure 6 for the study flow diagram. Reasons for exclusion included: adverse events not reported, outside of the scope of the review, commentary/letter/narrative review, no outcomes reported, not a clinical study, non-chiropractic, abstract/conference proceeding, non-English, and not reported in a peer-reviewed journal. Excluded studies are listed in Appendix 2.

Systematic reviews

Table 1 lists each item on the Risk of Bias assessment instrument of included SRs. Of the eight SRs included, four were of "*high quality*"[18, 76-78], two were of *"acceptable quality"*[70, 79], and two were of *"unacceptable quality"*[80, 81] and removed from analysis. Overall, only a qualitative analysis could be completed because of the lack of homogeneity between the trials (specifically regarding SMT) and limited methodological quality, as well as variation between individual studies (i.e., gestational age, number of participants, types of intervention, duration and frequency of intervention, outcome measures, and condition diagnosis). Table 2 summarizes the included SRs. One of the SRs examined a variety of treatment options[76] for the pregnant patient experiencing back pain, two examined osteopathic manipulative therapy (OMT)[77, 78], one assessed complementary and alternative medicine (CAM)[18] as a treatment option, one examined modalities[70] and the final SR looked at physical therapy[79] in general. The four *"high quality"* SRs recorded adverse events of which

Table 2.
Evidence table for SRs including treatment/intervention, quality rating, number and type of studies and overall study conclusions.

Citation and quality*	Treatment/ intervention	Number of studies and participants and type of studies	Adverse events reported	Overall study conclusion
Liddle 2015[76] High	Multimodal	34 studies (n=5,121): pertaining to: ***LBP*** 16 RCTs	The adverse event that were reported were considered transient and minor and mostly experienced by those who received acupuncture. ***LBP*** Overall, there were no serious adverse events to mother or fetus to report. *Exercise* (Group or individual): Studies reported no adverse events as a result of the intervention *Support devices:* No adverse events reported *Manual therapy*: One trial reported no adverse events; 1 trial reported that adverse events were similar amongst the groups, but no further details were given; 1 did not report on adverse events; 1 trial reported post-treatment soreness but no adverse effects as a result of the treatment *TENS:* No adverse event to report *Taping:* No adverse event reported	Overall, there is simply not good enough quality evidence to make confident decisions about treatments for these complaints. When reported, there were no lasting side effects on any of the studies. **LBP** There is low quality evidence that exercise improves pain and disability for women with LBP. Exercise interventions (from five to 20 weeks duration) improved the level of LBP and disability than women who just received regular prenatal care.
		PGP 6 RCTs	***PGP*** Overall, no long-lasting adverse effects were reported. *Acupuncture:* Data not provided on adverse events, but some Issues with needles (pain, bleeding, fainting). *Exercise + Education:* No adverse events reported *Belts:* Adverse effects not measured *Craniosacral Therapy:* some discomfort with belt, drowsiness and temporary increase in PGP	***PGP*** In general, there is less evidence on treatment for pelvic pain. There is evidence from single studies that suggesting that acupuncture or craniosacral therapy improved PGP more than usual prenatal care.
		Both LBP and PGP 12 RCTs	***Both LBP & PGP*** Overall, adverse events were minor and transient, when reported by subjects or investigators. There were no reported problems with any of the deliveries and neonates. *Acupuncture:* minor and transient adverse effects including bruising, local pain, nausea, weakness, heat or sweating *Physiotherapy:* some adverse effects, such as preterm uterine contractions, pre-eclampsia but unlikely to have been caused by physiotherapy	***Both LBP & PGP*** There is moderate quality evidence that exercise results in less sick leave and fewer women reporting pain. Although the results are variable, exercise (eight to 12 weeks duration) reduced the number of women who reported back pain and land-based exercises reduced sick leave in 2 studies. However, 2 other studies suggested that sick leave was no better at preventing LBP or PGP than usual care. In addition, there is evidence from low quality studies that multimodal care (manual therapy, exercise and education) reduced pain and functional disability, but not sick leave.
Franke 2017[78] High	OMT	8 RCTs* ***Pregnancy:*** 5 RCT ***Postpartum:*** 3 RCT *5 of 8 were grey literature	Only 1 of the studies reported on adverse events and they suggested that they were minor in nature; occasionally patients reported they were tired following treatment. In personal communication, authors of 2 other studies, they reported no adverse event occurred.	Clinically relevant effects of OMT were found for reducing pain and improving functional status in pregnant and postpartum (3 months posttreatment) women experiencing LBP.
Ruffini 2016[77] High	OMT	24 studies total but those pertaining to: ***Pregnancy*** 8 studies (n=914) 4 RCTs, 2 case controls, 1 observational study and 1 case-series	Overall, adverse events were not sufficiently described; only 3 studies mentioned adverse events. Researchers suggested a more systematic reporting of adverse events in order to obtain solid and generalizable results. ***Pregnancy*** *Craniosacral Therapy:* Minor events listed in the intervention group including increased PGP, elastic belt discomfort and drowsiness. Minor events listed in the control group including elastic belt discomfort and increases in PGP	OMT can be considered effective on pregnancy-related back pain.
		Labour and delivery 4 studies *(n=597)*: 1 RCT, 2 case-series and 1 observational study	***Labour and delivery*** Only reported adverse events in 2 studies and determined that OMT was well tolerated	
Hall 2016 High[18]	CAM	11 full text articles on 10 RCTs (n=1,198)	Researchers stated that their findings are similar to others in that very few adverse events have been reported in the literature and suggest complementary manual therapies are a safe option compared to no treatment at all.	There is limited evidence to support the use of complementary manual therapies as an option for managing LBP and PGP during pregnancy.
Gutke 2015[70] Acceptable	Modalities	34 RCTs; 8 CCTs; 3 long-term follow ups; 2 observational studies 4 observational retrospective studies; 1 experimental case study; 1 case series; and 3 pilot studies	No specific adverse events were recorded for any intervention (acupuncture, exercise, pelvic belt, physiotherapy, massage).	There was evidence for the positive effects of acupuncture and pelvic belts but weak for specific exercises.
Sharma, 2014[79] Acceptable	Physical therapy	9 RCTs; 1 cohort; 3 CS	No specific adverse events were recorded for any interventions (exercise, pelvic/sacroiliac belt, muscle energy techniques, soft tissue mobilization, postural alignment).	These authors recommend a combination of specific stabilizing exercises, nonelastic sacroiliac belt in the high position and ergonomic education as the most beneficial interventions in the management of sacroiliac dysfunction/PGP for pregnant individuals experiencing this pain.

Note: Majchrzycki (2015)[80] and Posadaski (2011)81 were deemed unacceptable and removed from the data extraction table.
*Scottish Intercollegiate Guideline Network (SIGN) Quality rating: >9=high quality, low risk of bias (H); 6-9=acceptable quality, moderate risk of bias (A); <6=low quality, high risk of bias (L)
CAM = complementary alternative medicine; CCT = controlled clinical trials; CS = case series; LBP = low back pain; OMT = osteopathic manipulative therapy; PGP = pelvic girdle pain;

Table 3.
Risk of bias assessment of included RCTs.

First author and year published	Items on Modified SIGN checklist[a]											
	1	2	3	4	5	6	7	8	9	10	Total	Quality[b]
Gausel, 2017	1	1	0	1	0	0	1	1	0	1	6	A
Schwerla, 2015[86]	1	1	1	1	0	1	0	1	1	1	8	A
Hensel, 2016[87]	1	1	0	1	1	0	1	1	0	0	6	A
Peterson, 2012[60]	1	1	0	1	0	0	1	1	1	1	7	A
Licciardone, 2010[83]	1	1	1	1	0	0	0	1	0	1	6	A
Licciardone, 2013[84]	1	1	1	1	0	1	1	1	1	1	9	A
Hensel, 2016[85]	1	1	0	0	0	1	1	1	0	0	5	L

RCTs = randomized controlled trials; SIGN = Scottish Intercollegiate Guideline Network
[a,b]See Figure 3 for Quality assessment SIGN checklist items[a] and scoring[b] for randomized controlled trials

almost all were considered transient and minor.[18, 76-78] In addition, one of the SRs stated that there were no issues related to any of the deliveries or neonates[76] and another suggested that CAM, such as chiropractic, was a safe option compared to no treatment at all for pregnancy-related back pain.[18] The two "*acceptable quality*" SRs[70, 79] did not record specific adverse events for any intervention they examined.

Randomized controlled trials

Table 3 lists each item on the Risk of Bias assessment instrument of included RCTs. Of the seven RCTs identified, six were of *"acceptable quality"*[60, 82-86] and one was of *"low quality"*.[87] Table 4 shows the data extraction of each RCT. There were five studies involving OMT[83-87] as the intervention, one study examining SMT[60], and one study which provided multimodal treatment[82]. Of the five studies that examined OMT, four were compared to sham or placebo ultrasound and/or usual obstetric care (UOBC)[83-85, 87] and one did not have a comparison group[86]. All of the studies that applied an OMT protocol to pregnant women in the third trimester did not report any specific adverse events with respect to worsening their back pain and/or an increase in poor labour and delivery outcomes.[83-85, 87] One study that examined the effects of OMT in women experiencing postpartum-related back pain did state that there were no serious adverse events reported, however occasionally participants did complain of being tired following the intervention.[86]

Two RCTs included SMT in their study design; one compared a multimodal approach including SMT to UOBC[82] and the other compared SMT and exercise to neuroemotional technique (NET) and a control group consisting of individual home exercises and information. Both of these studies asked patients to recall any negative reactions to treatment at the follow up visit. Both studies did not have any serious adverse or long-lasting events to report. However, the study involving SMT and exercise compared with NET did state that 6% and 18% of participants experienced soreness, respectively.

Cohort Studies

Table 5 lists each item on the Risk of Bias assessment instrument of included cohort studies. Of the cohort studies included two were of *"acceptable quality"*[88, 89], one was of *"low quality"*[90] and two were considered "*unacceptable quality*"[91,92]. The two "*unacceptable quality*" studies were removed. Table 6 shows the data extraction of each cohort study. In the first *"acceptable quality"* cohort study, it was determined that following a high velocity thrust technique (HVTT) for a maximum of two attempts per symptomatic side, 80% of participants reported an improvement of 50% or more within the first 24 to 72 hours following the intervention.[88] In this cohort study, no subject was determined to have greater disability or pain after the intervention.[88] The second *"acceptable quality"* cohort study examined chiropractic treatment (unspecified method or frequency, left up to the treating clinician) on pregnant women with LBP and/or PGP at one, three, six and 12 months following the start of treatment.[89] A large proportion of women undergoing chiropractic treatment reported clinically relevant improvements in their symptoms at all time points. Eighty-five percent of the participants were "very happy" or "happy" with their

Table 4.

Evidence table for RCTs including quality rating, patient information, intervention and comparison group, dosage, adverse events reported and study conclusions.

Citation and quality*	Patient population, mean age, mean symptom duration	Intervention	Comparison group(s)	Dosage	Adverse event reported	Conclusion
Gausel 2017[82] Acceptable	N=56, pregnant women, less than 29 wks, with 1-sided PGP Age (mean yrs): TG: 28.9 CG: 29.9 GA (mean wks): 23.1 Onset: Prior to 18-29 wks	TG: SMT, mobs, STT, exercises and advice chosen by the chiropractor	CG: UOBC	TG: Number of treatments individualized by the chiropractor	Reported: At follow-up appts, women were asked to recall any negative reactions. No serious or long-lasting adverse events were reported. Although adverse events following SMT during pregnancy are rare, treatments should not be performed over a long period of time unless there is a positive response. Future studies should track possible adverse events throughout the study.	There were no statistically significant differences between the treatment group and control group with respect to sick leave, pain, disability or general health status.
Schwerla 2015[86] Acceptable	n=80, postpartum women with nonspecific LBP or PGP; at least 3mo and 5/10 on VAS Age (Mean wk): TG=33.9 CG=33.3 GA: TG= postpartum CG= postpartum Onset: Within the past 3 to 15 mo Duration: TG: 9.8 mo CG: 9.7 mo	TG: OMT could include direct and indirect visceral and cranial techniques	CG: No tx but told they were put on a wait list to be scheduled 2 mo later	8 wks 4 txs 40-60 min	Reported: No serious adverse events were recorded during the study period. Occasionally, participants complained of being tired following the intervention.	OMT applied 4 times to postpartum women led to clinically relevant positive changes in pain intensity and functional disability.
Licciardone 2010[83] Acceptable	n=146, pregnant women, third trimester with or without LBP Age (Mean yrs) TG=23.8 CG1=23.7 CG2=23.8 GA: Enrolled 28-30 wks Onset: Not stated. Duration: Not stated.	TG: UOBC + OMT: Standardized OMT protocol during 3rd trimester	CG1: UOBC + SUT CG2: UOBC	Up to 7 treatment in conjunction with OB appointments at 30, 32, 34, 36, 37, 38 and 39 wks gestation 30 min	No specific adverse events reported. But the authors stated that the study demonstrated important clinical benefits without any appreciable harms in back-specific functioning when OMT is provided as complementary therapy in the third trimester.	OMT does halt or lessen back pain during the third trimester of pregnancy; however the possibility of minimally important harms cannot be ruled out.
Hensel 2016[87] Acceptable	n=400, pregnant women, 3rd trimester Age (Mean yrs): TG=24.0 CG1=24.1 CG2=24.7 GA: Enrolled at 30 wks Onset: Not stated Duration: Not stated	TG: OMT= Usual care + standardized OMT protocol	CG1: PUT CG2: UOBC	OMT and PUT groups provided 7 visits within 24 hours of OB visit 20 min over 9 wks	No specific adverse events reported. The authors did state that the OMT protocol did not increase the risk of precipitous labour, conversion to cesarean delivery or meconium-stained amniotic fluid Although the OMT group experienced longer labour, there was no increased incidence of complications during delivery including perineal laceration, episiotomy or need for forceps or vacuum	Those who received OMT protocol in addition to usual care had a slower rate of deterioration of their pain and back-specific functioning during the third trimester. The OMT protocol appears to be a safe and effective way to manage back pain and function during pregnancy.
Hensel 2016[85] Low	n=400, pregnant women, 3rd trimester Age (Mean yrs): TG=24.1 CG1=24.1 CG2=24.8	TG: OMT= Usual care + standardized OMT protocol	CG1: PUT CG2: UOBC	OMT and PUT groups provided 7 visits within 24 hours of OB visit 20 min over 9 wks	No specific adverse events reported. When using high-risk status and labour and delivery outcomes as an index for safety, no greater risk in the OMT group was found.	The OMT protocol applied in the third trimester of pregnancy, is a safe intervention with respect to labour and delivery outcomes.
Peterson 2012[60] Acceptable	n = 57, pregnant women with LBP and/or PGP reproducible by palpation Age: TG1= 31.1 TG2=29.7 CG= 28.7 GA: TG1= 25.7 TG2= 27.0 CG=23.7 Onset: TG1=16.1 TG2=13.9 CG=11.6 Duration: During pregnancy	TG1: SMT= HVLA for L/S and SI JT; blocks used to adjust Sacro Occiptial Technique Category II pelvis; activator to adjust pelvis TG 2: NET= chiropractic mind-body technique; combines desensitization procedures with 5 element Chinese medicine + chiropractic adjustment	CG: Individualized home exercises + Information	All TGs: Paralleled prenatal care schedule; 1x/mo until 28 wks; 2x/mo until 36 wks; 1x/wk thereafter CG: 5 x/wk 15 min	Reported: Participants were asked at each assessment if they experienced any adverse events as a result of the intervention. No adverse events were reported but the study participants in any group. However, 6% of SMT and exercise and 18% of NET participants produced soreness	All 3 interventions appear to provide clinically meaningful improvements in function and pain intensity.
Licciardone 2013[84] Acceptable	N= 144, pregnant women in 3rd trimester with or without LBP Age: TG: 23.8 CG1: 23.7 CG2: 23.8 GA: enrolled between 28 -30 wks Onset: not stated Duration: not stated	TG: OMT + UOBC	CG1: SUT + UOBC CG2: UOBC	Up to 7 treatment in conjunction with OB appointments at 30, 32, 34, 36, 37, 38 and 39 wks gestation 30 min	No adverse events specifically reported. The authors did state that there was no SS between study groups in the rates of development of high-risk obstetric conditions or delivery prior to wk 39	OMT has medium to large treatment effects in preventing progressive back-specific dysfunction during the 3rd trimester.

*Modified Scottish Intercollegiate Guideline Network (SIGN) Quality RCT rating: 9-10 high quality, low risk of bias; 6-8 acceptable quality, moderate risk of bias; 3-5 low quality, high risk of bias; 0-2 or if item 1 and/or 3 are "no unacceptable quality (reject)

CG – control group; GA – gestational age; HVLA – high velocity low amplitude; LBP – low back pain; L/S – lumbar spine; min – minute; mo – month; mobs – mobilization; NET = neuroemotional technique; OB – obstetrician; OMT – osteopathic manipulative therapy; PUT – placebo ultrasound therapy; SI JT – sacroiliac joint; SMT – spinal manipulative therapy; SS = statistial significance; STT – soft tissue therapy; SUT – sham ultrasound therapy; TG – treatment group; tx – treatment; txs – treatments; UOBC – usual obstetric care; wk – week; wks – weeks; x/ – times per; yrs – years

Table 5.

Risk of bias assessment of included cohort studies.

First author and published year	Items on SIGN checklist															
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total	Quality[b]
Al-Sayegh, 2010[88]	1	1	1	0	1	0	1	0	0	1	1	0	0	1	8	A
Peterson, 2014[89]	1	0	0	0	1	0	1	0	1	1	1	1	1	0	8	A
Hastings, 2016[90]	1	0	1	0	0	0	1	0	1	1	1	0	1	0	7	L
Skarica, 2018[92]	1	0	0	0	0	0	1	0	0	0	0	0	0	0	2	U
Haavik, 2016[91]	1	0	0	0	0	0	1	1	0	0	0	0	1	0	4	U

SIGN, Scottish Intercollegiate Guideline Network
[a,b]See Figure 4 for Quality assessment SIGN checklist items[a] and scoring[b] for cohort studies

Table 6.

Evidence table for cohort studies including quality rating, patient information, intervention, dosage, adverse events reported and study conclusions.

Citation and quality*	Patient population, mean age, mean symptom duration	Intervention	Dosage	Adverse event reported	Overall study conclusion
Al-Sayegh 2010[88] Acceptable	n=69, postpartum women with LBP and/or PGP Age (Mean yrs): All: 31 TG1: 30 TG2: 34 GA: Postpartum Onset: Anytime during pregnancy or postpartum Duration: All: 28.9 wks TG1: 28.8 wks TG2: 29.9 wks	All subjects HVTT + forward rocking G1: HVTT success G2: HVTT non-success	2 attempts at each visit	Reported: In no case was a subject determined to have greater disability or pain after the intervention.	The pretest probability of success (80%) is enough to reassure the clinician about the decision to use HVTT lumbopelvic region in postpartum women experiencing LBP and/or PGP
Peterson 2014[89] Acceptable	n=143, pregnant women with LBP, PGP or both Age (mean yrs): 32.96 GA (mean wks): 26.21	Chiropractic treatment (unspecified)	Was left to the discretion of the treating clinician	Reported: No adverse events were reported and 85% of patients were happy or very happy with their chiropractic treatment.	A large proportion of patients with LBP or PGP undergoing chiropractic treatment reported clinically relevant improvements in their symptoms at all time points up to 1 yr.
Hastings 2016[90] Low	n= 75-80 pts approached, women who delivered within 48 hrs Age: not reported GA: postpartum	OMT – based on somatic dysfunction;	Was left to the discretion of the treating clinician; 20-30 min; most commonly used myofascial release, balanced ligamentous tension and facilitated positional release	Reported: Slight increase in tenderness and sharpness immediately following OMT, although not SS, is consistent with what is already reported in the literature. It is believed to result from minor and temporary tissue irritation	Most postpartum patients undergoing chiropractic treatment reported clinically relevant improvements at all time points.

Note: Skarica (2018)[92] and Haavik (2016)[91] were deemed unacceptable and removed from the data extraction table.
*Scottish Intercollegiate Guideline Network (SIGN) Quality rating: 12-14 high quality, low risk of bias; 9-11 acceptable, moderate risk of bias; 6-8 low quality, high risk of bias; <6 unacceptable quality
G = group; GA = gestational age; hrs = hours; HVTT = high velocity thrust technique; LBP = low back pain; min = minute; OMT = osteopathic manipulative therapy; PGP = pelvic girdle pain; pts = patients; SS = statistically significant; TG = target group; wks = weeks; yr = year

Table 7. *CARE Case studies*

		Morton, 2012[93]
1.	Title	1
2.	Key Words	1
3.	Abstract	
a.	Introduction	1
b.	Patient's main concerns and important clinical findings.	1
c.	The main diagnoses, intervention and outcomes.	1
d.	Conclusion – what are the "take away" lessons?	1
4	Introduction	1
5	Patient information	
a.	De-identified demographic and other patient information.	1
b.	Main concerns of the symptoms of the patient.	1
c.	Medical, family and psychosocial history including genetic information.	1
d.	Relevant past interventions and their outcomes.	0
6.	Clinical findings	0
7.	Timeline	0
8.	Diagnostic Assessment	
a.	Diagnostic methods (PE, laboratory testing, imaging, surveys)	0
b.	Diagnostic challenges	N/A
c.	Diagnostic reasoning including differential diagnosis	N/A
d.	Prognostic characteristics when applicable	N/A
9.	Therapeutic Intervention	
a.	Types of intervention (pharmacologic, surgical, preventive)	0
b.	Administration of intervention (dosage, strength, duration)	0
c.	Changes in the intervention with explanations	N/A
10.	Follow up and Outcomes	
a.	Clinician and patient-assessed outcomes when appropriate.	0
b.	Important follow-up diagnostic and other test results.	1
c.	Intervention adherence and tolerability (how was this assessed).	N/A
d.	Adverse and unanticipated events.	1
11	Discussion	
a.	Strengths and limitations in your approach to the case.	0
b.	Discussion of the relevant medical literature.	1
c.	The rationale for your conclusion.	1
d.	Primary "take-away" lessons from this case report.	1
12	Patient perspective	0
13.	Informed consent	1
	Total	16
	Adverse events Reported	Yes

treatment and the authors reported that no adverse events had occurred.[89] The final cohort study of *"low quality"* determined the effects of a 20 to 30 minute OMT treatment on women who delivered within 48 hours. Although their preliminary results suggested that OMT is efficacious for postpartum pain management, 18.6% of participants experienced a slight increase in tenderness and sharpness immediately following their treatment.[90]

Case studies

Table 7 lists each item on the CARE checklist.[75] Only one case study[93] reported a serious adverse event following SMT on the cervical spine in a 16 week pregnant woman (Table 8). Immediately following a cervical SMT treatment the patient experienced right-sided anterior neck pain and developed ipsilateral Horner's syndrome as a result of a dissection of the right internal carotid artery. Four days following the treatment, the patient miscarried. The patient was admitted to the ICU and treated accordingly. One year later, the Horner's symptoms still persisted.

Discussion

This systematic review provides an update of the literature regarding SMT during pregnancy and the postpartum period, as well as a review of any adverse events associated with the reported studies. With the exception of one case study, all studies reported only minor and transient events. The case study demonstrated an adverse event following cervical spinal manipulation. When added to the results of our 2012 review (four events following cervical SMT and three events following lumbar SMT) adverse events following SMT in these populations still appear to be scarce.

Table 8.

Evidence tables for case studies including citation, case presentation and treatment and reported adverse events.

Citation	Case Presentation	Treatment and Adverse Event reported
Morton, 2012	A 31-yr old woman presented to the chiropractor at 16-wks GA with occipital HA. She has a 17-yr previous history of monthly, intermittent, bilateral occipital muscle tension HA that are unchanged with pregnancy. In addition, she had a history of migraine characterized by unilateral frontal HA, the last episode which had been 6-wks earlier. Patient was diagnosed with SLE 12 yrs earlier, complicated by renal involvement treated with azathioprine and prednisone, hypertension managed with labetalol and episodes of DVT and PE. She was heterozygous for prothrombin gene mutation but did not have lupus anticoagulant or anticardiolipin antibody.	Immediately following chiropractic treatment (not specified but based on description, SMT was suggested), the subject reported severe right-sided anterior neck pain and developed ipsilateral Horner's syndrome. MRI revealed dissection of the right internal carotid artery. It extended 5 cm distal to the carotid bulb to the horizontal intrapetrous segment. SLE flared up. 4 days after the onset of neurological symptoms, intrauterine fetal demise occurred. Tx: reported to ICU and treated with intravenous heparin and subsequently low-molecular weight heparin. Patient was placed on warfarin for 6 months. A follow-up MRI revealed a focal false aneurysm on the right internal carotid artery. One year later, Horner's syndrome persists.

cm – centimetre; DVT – deep vein thrombosis GA – gestational age; HA – headache; ICU – intensive care unit; MRI – magnetic resonance imaging; PE – pulmonary embolism; SLE – systemic lupus erythematosus; SMT – spinal manipulative therapy; Tx - treatment; yrs – years;

One important revelation in this review is the lack of adverse events being reported, which was also highlighted in a few of the studies included in this review.[77, 82] Tracking of adverse events was not common practice in higher quality studies, such as RCTs, until the CONSORT guidelines[94, 95] were developed and changed over the years to encourage researchers to do so. Unfortunately, the reporting of adverse events is a missing component of research papers. In the current paper, the fact that very few adverse events were reported, does not mean that others did not happen. There has to be a greater effort made by researchers to report not only adverse events associated with studies but also to clearly state that no adverse events occurred when that is the case. Future research should not only focus on reporting the presence or absence of adverse events,[76] but also determining the adverse events that occur at each of the different pain locations experienced by pregnant and postpartum patients. Recently, there has been a greater emphasis on delineating the various pain locations (lumbar spine LBP versus PGP versus combined pain) experienced by pregnant and postpartum patients.[57,58,76,96,97] Robust trials on the effectiveness of SMT for cervical and thoracic spine in these populations are required to help inform decisions regarding care. By utilizing all of this information, future studies can be designed and ultimately determine possible prevention and effective management strategies for these populations.

Chiropractors are well versed in treating pregnant and postpartum patients.[59] However, the evidence with respect to safe and effective treatment options, including SMT, in these patients is limited. Two recent SRs regarding pregnancy[58] and postpartum-related back pain[57] have suggested that SMT should be considered as a possible modality to treat these two populations. Although the strength for SMT in these two SRs was inconclusive, it has been suggested that a trial of care may be warranted to see if it produces symptomatic relief for patients.[4, 57, 58] Determining conclusive evidence in these populations may be difficult simply because of the rarity of these events.[93] In one RCT examining the effects of a multimodal program including SMT on LBP the authors suggest that although adverse events during pregnancy are rare, treatments should not be performed unless there is a positive response within a trial of care period.[82] Unfortunately, there is even less evidence with respect to the safety and suggested treatment strategies for neck pain during the pregnant and postpartum period.

We continue to support the suggestions from our previous review:[69] (1) that contraindications to SMT are evident during a careful history and physical exam; (2) clinicians treating these two populations should consider prothrombotic and joint laxity risk factors when determining their treatment plan and attempt to minimize the risk of potentially dangerous and neurological complications; and (3) pregnant and postpartum women at higher risk for complications, such as those in a post-thrombotic state or possible joint laxity, should be treated with additional caution. These patients should be counselled with respect to the risks of SMT and educated as to the signs and symptoms of possible neurovascular complications.[69] In addition, we believe that future studies should include the presence or absence adverse events. Reporting this information will help to inform stakeholders of the actual possible adverse events that may occur in these populations.

Strengths and limitations

A key strength of this review is that a thorough search of the literature was conducted by a health science librarian, multiple electronic databases were searched, and we employed a number of broad search terms. Another strength for this review is that we expanded our search to include all forms of literature including SRs and meta-analyses, RCTs, cohort and case studies. In general, the information garnered in this paper should provide practicing chiropractors, chiropractic educators, chiropractic patients and other allied health professionals a reasonable and evidence-based rationale to the safety of SMT in these two populations.

There are a few limitations associated with this review. The first is the number of studies available and the hierarchy of available evidence. Similar to our 2012 review, the majority of the papers identifying serious adverse events were case studies, and they are considered lower levels of evidence because of their high risk of bias. The second limitation is the reporting of adverse events, or lack thereof in clinical trials. In most of the papers included in this review there was no mention of whether or not an adverse event occurred following treatment. Similar to the limitations of our previous review, we suggest that given the lower levels of evidence and the lack of reporting

of adverse events, the possibility of risk to pregnant and postpartum undergoing SMT cannot be measure or stated definitively. In addition, it cannot be determined if any such risk level is higher or lower than in non-pregnant or postpartum populations. There is a need to execute more robust high-quality studies, such as the SafetyNET active surveillance reporting system,[98, 99] to rigorously track adverse events and potentially develop mitigation strategies in these populations. The third limitation is the time frame since the current search was completed. Although it has been two years since the last search, similar to what we found between the original study and the current one, we do not anticipate any major changes with respect to the reporting of adverse events. However, a future update will be completed in a more expedient manner. The final limitation is the restriction of our postpartum timeline of six weeks. The hormonal changes that occur with pregnancy do not automatically revert back to a pre-pregnancy state with birth of a child. Therefore, we maybe limiting the number of studies that could have been retrieved and the adverse events associated with them. Extending the postpartum timeline should be considered for a future update.

Conclusions

High quality studies, such as RCTs, regarding SMT for pregnancy- and postpartum-related spinal pain are lacking. This update of our previous review found one case study[93] that demonstrated a serious adverse event following SMT in the cervical spine and a handful of minor and transient adverse events in the low back[18, 60, 76, 77, 86]. Although we are calling for improved reporting of such events in all papers going forward, it appears these events are rare. Future research should focus on the proper reporting of all adverse events while assessing efficacy of appropriate treatment options for these populations.

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Appendix 1.
Search strategy terms

MEDLINE

1. MH "Long Term Adverse Effects"
2. adverse event*
3. adverse reaction*
4. adverse effect*
5. side effect*
6. TI harm* or AB harm*
7. (increas* n2 pain*) or (incident* n2 pain*)
8. hematoma*
9. sprain* or strain*
10. (disc n2 herniat*) or (disk* n2 herniat*)
11. (disc n2 bulg*) or (disk* n2 bulg*)
12. thrombophil* or thrombosis* or hypercoag*
13. dissection*
14. stroke*
15. fractur*
16. MH Chiropractic
17. MH Manipulation, Spinal
18. MH Musculoskeletal Manipulations
19. MH Manipulation, Chiropractic
20. chiroprac*
21. spinal* n2 manip*
22. spinal* n2 adjust*
23. musculoskeletal n2 manip*
24. musculoskeletal* n2 adjust*
25. manual n2 therap*
26. manual* n2 adjust*
27. hvla
28. high velocity low amplitude* or high-velocity low-amplitude* or high velocity thrust* or high-velocity thrust*
29. audibl* n2 releas*
30. subluxat*
31. MH Pregnancy
32. MH Pregnant Women
33. MH Pregnancy Outcome
34. MH Pregnancy Complications
35. MH Prenatal Care
36. MH Postpartum Period
37. MH Parturition
38. pregnan*
39. childbirth*
40. antenatal* OR ante natal* OR ante-natal*
41. prenatal* OR pre natal* OR pre-natal*
42. postnatal* OR post natal* OR post-natal*
43. postpartum* OR post partum* OR post-partum*
44. perinatal* or peri natal* or peri-natal*
45. peirpartum* or peri-partum*
46. 1-15/ OR
47. 16-30/ OR
48. 31-45/ OR
49. 46 AND 47 AND 48
50. LIMIT English
51. LIMIT January 1 2010-Nov 1 2018