Osteopathic manipulative treatment for low back and pelvic girdle pain during and after pregnancy: A systematic review and meta-analysis

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ABSTRACT

Background: To examine the effectiveness of osteopathic manipulative treatment (OMT) for low back pain (LBP) in pregnant or postpartum women.

Methods: Randomized controlled trials unrestricted by language were reviewed. Outcomes were pain and functional status. Mean difference (MD) or standard mean difference (SMD) and overall effect size were calculated.

Results: Of 102 studies, 5 examined OMT for LBP in pregnancy and 3 for postpartum LBP. Moderate-quality evidence suggested OMT had a significant medium-sized effect on decreasing pain (MD, -16.65) and increasing functional status (SMD, -0.50) in pregnant women with LBP. Low-quality evidence suggested OMT had a significant moderate-sized effect on decreasing pain (MD, -38.00) and increasing functional status (SMD, -2.12) in postpartum women with LBP.

Conclusions: This review suggests OMT produces clinically relevant benefits for pregnant or postpartum women with LBP. Further research may change estimates of effect, and larger, high-quality randomized controlled trials with robust comparison groups are recommended.

Keywords: Low back pain, pregnancy, postpartum, spinal manipulation, osteopathic manipulative treatment, systematic review
BACKGROUND

Low back pain (LBP) and posterior pelvic pain (PPP) are common during pregnancy (Vermani et al 2010) and often remain a disabling problem postpartum (Wu et al 2004). The prevalence of LBP in pregnancy ranges from 24%-90%, although it is most commonly estimated at 40%-50% (Gutke et al 2008b, Vermani et al 2010, Vleeming et al 2008). Prevalence increases with the duration of pregnancy and is at the highest point in the third trimester (Ostgaard et al 1994, Sabino & Grauer 2008). The prevalence of LBP in postpartum women increases in the year after delivery, with estimates from 28% after 3 months to over 50% after 5 months and 67% after 12 months (Brown & Lumley 1998, MacArthur et al 1991, Patel et al 2007, Saurel-Cubizolles et al 2000).

LBP is defined as pain in the lumbar region located below the costal margin and above the inferior gluteal folds (van Tulder et al 2006). PPP has been defined as pain in the symphysis pubis and/or pain in the regions of one or both sacroiliac joints and pain in the gluteal region (Vermani et al 2010, Wu et al 2004). Much of the literature on pregnancy-related back pain has not distinguished between LBP and PPP and both will be referred to as LBP in this review.

The cause of LBP during pregnancy is unclear and appears to be nonspecific and may be related to changes in body posture with increased lumbar lordosis to balance the increasing anterior weight of the abdomen. These postural changes, in combination with inefficient neuromuscular control, may contribute to the development of joint, ligament, and myofascial dysfunctions (Gutke et al 2008a, Majchrzycki et al 2010, Vleeming et al 2008). Similarly, the cause of PPP is unclear, but the term implies the origin is from a musculoskeletal source, such as the pubic symphysis or sacroiliac joints, rather than pelvic viscera. Mechanical, traumatic, hormonal, and degenerative factors have all been proposed as causes of PPP, but all are speculative (Vermani et al 2010).

European guidelines recommend that pregnancy-related LBP should be managed by providing adequate information and reassurance to stay active, continue normal daily activities and work, and offer individualised exercises where appropriate (Vleeming et al 2008). In a recent Cochrane review, Liddle and Pennick (Liddle & Pennick 2015)
reported that there was low-quality evidence that exercise may reduce pregnancy-related LBP and functional disability. The authors stated there was evidence from single studies which suggested that acupuncture, osteopathic manipulative therapy, and multi-modal interventions (manual therapy, exercise, and education) may be of benefit.

Osteopathy is a health approach that emphasizes the role of the musculoskeletal system in health and promotes optimal function of the tissues of the body by using a variety of manual techniques (DeStefano 2012, DiGiovanna et al 2005). Osteopathic manipulative treatment (OMT) typically involves an eclectic range of manual techniques, which may include soft tissue stretching, spinal manipulation, resisted isometric ‘muscle energy’ stretches, and visceral technique. Treatment is characterised by a holistic approach to the patient and may include lifestyle advice and biopsychosocial approaches as part of patient management (Vaughan et al 2014). OMT is typically applied to many regions and tissues of the body, sometimes remote from the symptomatic area, at the clinical judgement of the practitioner (DeStefano 2012, DiGiovanna et al 2005, Vaughan et al 2014).

There is growing evidence that OMT may be beneficial for treatment of women with pregnancy-related or postpartum LBP (Franke et al 2014, Majchrzycki et al 2015). Majchrzycki et al. (Majchrzycki et al 2015) reviewed the literature and concluded that OMT appears to be safe and effective treatment for pelvic and spinal pain in pregnant women. However, this review mixed studies of different designs, included duplicate data from the same study (Licciardone & Aryal 2013, Licciardone et al 2010), and included both OMT and non-osteopathic manual therapies, so the conclusions should be viewed with caution. In a systematic review of the effectiveness of OMT for nonspecific LBP, Franke et al. (Franke et al 2014) reported low-quality evidence (downgraded due to inconsistency and imprecision) supporting OMT for LBP pain and functional status in pregnant women and moderate-quality evidence for pain and functional status in postpartum women. However, this evidence was limited by the low number of available studies, low participant numbers, inconsistency in the results, and different comparison groups between studies (Franke et al 2014).
The aim of the current review is to update the evidence for the treatment of pregnancy-related and postpartum LBP with OMT since the last review (Franke et al 2014). As recommended by the Cochrane Collaboration (Higgins & Green 2011), the current review searched the non-published ‘grey’ literature and was not restricted by language in order to retrieve all available studies.

METHODS

Criteria for considering studies for the current review

types of studies

Only randomized controlled trials (RCTs) were included in the current review. Potential studies could be published or unpublished (grey literature) in any language.

types of participants

We included studies with pregnant or postpartum adults (older than 18 years and with postpartum defined in these studies from 3-24 months following delivery) with nonspecific LBP (i.e., pain between the lumbo-pelvic region and the 12th rib) and/or PPP (pain in the symphysis pubis and/or pain in the regions of one or both sacroiliac joints and pain in the gluteal region) without any limitation of the duration of the pain period (acute, subacute, or chronic back pain). We excluded studies which included participants with specific LBP or PPP (back pain with a specific cause, e.g., compression fracture, a tumour or metastasis, ankylosing spondylitis, infection).

types of interventions

Treatment was required to be an ‘authentic’ OMT intervention where the practitioners were identified as osteopaths or osteopathic physicians and had a choice of manual techniques and judgment was required for the treatment selection, without any technique restrictions or standardized treatment protocols. The techniques chosen were based on the treating examiner’s opinion of what techniques would be most appropriate for a given patient. This eclectic, pragmatic approach best represents ‘real-world’ osteopathic practice (Fryer et al 2010, Johnson & Kurtz 2003, Orrock 2009), as opposed to treatment following an established study protocol that applies an isolated manual technique or set of techniques.
Therefore, our inclusion criteria were RCTs of OMT for nonspecific LBP in pregnant or postpartum women where the treating practitioner was an osteopath or osteopathic physician who used clinical judgment to determine the treatment performed. Only studies where an effect size could be assigned to the OMT intervention were considered. If co-interventions were used, they also had to be performed in the control group. Studies were excluded that used an intervention of a single manual technique, such as high-velocity manipulation.

**types of comparisons**
Studies with any type of comparison group (e.g., manual therapy, usual care, sham treatment, untreated) were included.

**types of outcome measures**
Only patient-reported outcome measures were evaluated.

**Primary outcomes**
The primary outcomes were pain and functional status. Pain was measured by visual analogue scale (VAS), number rating scale (NRS), or the McGill Pain Questionnaire. Studies measured functional status using the Roland-Morris Disability Questionnaire, Oswestry Pain Questionnaire, Pelvic Girdle Pain Questionnaire, or another valid instrument. For the meta-analysis, the outcome measure (pain or functional status) of the last treatment time point was used.

**Secondary outcome**
These outcomes included any kind of adverse event.

**Data sources and searches**
A systematic literature search was performed in December 2016 in the following electronic databases: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, CINAHL, PEDro, OSTMED.DR, and Osteopathic Web Research. The following search terms were used: low back pain, back pain, lumbopelvic pain, dorsalgia, osteopathic manipulative treatment, OMT, osteopathic medicine, pregnancy, and postpartum. In addition to the listed databases, an ongoing trial database was also screened (metaRegister of Controlled Trials [http://controlled-}
trials.com/mrct). Our search was supplemented by citation tracking of the identified trials and a manual search in the reference lists for all relevant papers that were not listed in the electronic databases. This search strategy was the same as a previous review (Franke et al 2014) but used the additional terms: “Pregnancy”[Mesh] and “Postpartum Period”[Mesh]. Table 1 shows an example of the applied search strategy in MEDLINE.

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Study selection
Three authors independently screened titles and abstracts of the results identified by our search strategy. Potentially eligible studies were read in full text and independently evaluated for inclusion in the current review.

Data extraction and quality assessment
Two authors independently extracted data from identified studies using a standardized data extraction form.

Dealing with missing data
If the article did not contain sufficient information, the authors were contacted for additional information. When standard deviations (SDs) were not reported, we estimated these from the confidence intervals (CIs) or other measures of variance, where possible.

Assessment of heterogeneity
Heterogeneity refers to the variation in study outcomes between studies and is useful for the interpretation of meta-analysis results. Assessment of heterogeneity was based on the calculation of I². The Cochrane Collaboration (Higgins & Green 2011) provides the following interpretation of I²: 0% to 30%, might not be important; 30% to 60%, may represent moderate heterogeneity; 50% to 90%, may represent substantial heterogeneity; and 75% to 100%, considerable heterogeneity.

Unit of analysis issues
In cases where 3 or more interventions were evaluated in a single study, we included each pair-wise comparison separately. In these instances, the total number of participants in the OMT intervention group was divided approximately evenly among the comparison groups.

Assessment of risk of bias in included studies
The methodological quality of the studies was assessed using the Risk of Bias tool of the Cochrane Back Review Group (Furlan et al 2009). Discussion and consensus between the researchers were used to resolve disagreements about the methodological quality of the RCTs included in the current review. Every Risk of Bias criterion was scored as ‘low risk’, ‘high risk’, or ‘unclear’ and included assessment of randomization, blinding, baseline comparability between groups, patient compliance, and dropping out. In line with recommendations from the Cochrane Back Review Group, studies were rated as having ‘low risk’ when at least 6 criteria were met and the study had no serious flaws (e.g., large dropout rate). A dropout rate of greater than 20% for short-term follow-up and 30% for long-term follow-up was defined as a serious flaw and the comparison was excluded from quantitative analysis. When information was missing from the published studies and the authors could not be contacted or when the information was no longer available, the criteria were scored as ‘unclear’.

Measures of treatment effect
Data for the meta-analysis was analysed using Review Manager (RevMan, Version 5.3., Nordic Cochrane Centre, http://ims.cochrane.org/revman). For measurement of pain, the NRS or VAS scores from the included studies were converted to a 100-point scale and the mean difference (MD) with 95% CIs was calculated in a random effects model. For functional status, the standard mean difference (SMD) was also used in a random effects model. The studies were grouped into 2 groups for meta-analyses: LBP in pregnant women and LBP in postpartum women. Further, subgroup analyses were conducted to examine OMT versus each specific intervention and to determine if there were differences in effects of the published and unpublished studies.

Assessment of clinical relevance
Assessment of clinical relevance was made using the recommendations of the Cochrane Back Review Group. Therefore, we defined a small effect as MD less than 10% of the scale (e.g., 10 mm on a 100 mm VAS) and SMD or ‘d’ scores less than 0.5. A medium effect was defined as MD 10% to 20% of the scale and SMD or ‘d’ scores from 0.5 to 0.8. A large effect was defined as MD greater than 20% of the scale and SMD or ‘d’ scores greater than 0.8 (Furlan et al 2009).

Data synthesis
The overall quality of the evidence for each outcome in the included studies was assessed using the GRADE approach (Guyatt et al 2011, Kunz et al 2008), as recommended by the updated Cochrane Back Review Group method guidelines (Furlan et al 2009). The GRADE approach specifies 4 levels of quality, the highest rating being for RCT evidence. Authors of systematic reviews can downgrade this evidence to moderate, low, or even very low quality evidence, depending on the evaluation of quality of the evidence for each outcome against 5 key domains, which are (1) limitations in design (downgraded when more than 25% of the participants were from studies with a high risk of bias), (2) inconsistency of results (downgraded in the presence of significant statistical heterogeneity and inconsistent findings), (3) indirectness (i.e., generalizability of the findings, downgraded when more than 50% of the participants were outside the target group), (4) imprecision (downgraded when the total number of participants was less than 400 for each continuous outcome), and (5) other (such as publication bias) (Rubinstein et al 2011).

For the current review, the following quality definitions were followed. For high-quality evidence, further research was very unlikely to change our confidence in the estimate of effect. There were also consistent findings among at least 75% of RCTs with no limitations of the study design and no known or suspected reporting biases. For moderate quality, further research was likely to have an important impact on confidence in the estimate of effect and may have changed the estimate; 1 of the domains was not met. For low quality, further research was very likely to have an important impact on confidence in the estimate of effect and was likely to change the estimate; 2 of the domains were not met. For very low quality, there was great uncertainty about the estimate; 3 of the domains were not met. For no evidence, no
RCTs were identified that addressed the outcome. The research methods and reporting of this study adhered to the PRISMA guidelines (Liberati et al 2009).

RESULTS

Included studies


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Excluded studies

Following examination of the study titles, 13 of the identified 102 studies were read in full text. Five of these studies were excluded for various reasons. One publication (Licciardone & Aryal 2013) used the same data as another included study (Licciardone et al 2010). The other 4 studies were excluded because they were not RCTs (Carpenter & Woolley 2001, Close et al 2014, Kofler 2006, Majehrzycki et al 2015).

Risk of bias

All of the included studies in the review were judged to have high internal validity (low risk of bias) where studies were rated as having ‘low risk’ when at least 6 criteria were met and the study had no serious flaws (Furlan et al 2009) (Table 3). For each of
the 3 blinding criteria every study was deemed to be high risk, which is typical of most manual therapy studies.

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Effect of interventions
Results are presented in the forest plots (Figures 1-4) and in the summary of findings tables (Tables 4 & 5). All results are based on measures at the time of the last treatment time point. For the treatment of postpartum LBP, the final time point for each study was 8 weeks, which was a point 2 weeks after the last treatment session (Belz 2014, Recknagel & Roß 2007, Schwerla et al 2015). For treatment of LBP in pregnancy, there was more variation. In 2 studies, the final time point was also 8 weeks, 2 weeks after the last treatment session (Gundermann 2013, Röhrich 2014). In another study (Licciardone et al 2010), the final time point was 9 weeks, directly after the last treatment, and in another (Peters & van der Linde 2006) it was 4 weeks, 1 week after the last treatment. Hensel et al. (2015) are less specific because this study was scheduled for 7 treatment visits to correspond with ongoing routine prenatal care at weeks 30, 32, 34, 36, 37, 38, and 39. The authors stated that 99 women completed the full 7 visits, but 357 women completed at least 4 of the scheduled 7 visits. In addition to a drop-out of 20% because of participants who became ineligible or declined to continue, additional attrition was related to delivery earlier than 39 weeks of gestation (Hensel et al. 2015). This was considered to be a valid end point for the review, and the data was included in the current analysis.

OMT for low back and posterior pelvic pain during pregnancy
Five studies with 7 comparison groups and 677 participants were analyzed for effect of OMT on LBP during pregnancy. Four of the 7 comparisons were reported as having significant effects in favor of OMT for pain (Gundermann 2013, Hensel et al 2015, Peters & van der Linde 2006, Röhrich 2014), whereas 2 showed non-significant effects in favor of OMT (Licciardone et al 2010), and 1 comparison had non-significant effects in favor of the control (Hensel et al 2015). For functional status, 4 of the comparisons were reported as having significant effects in favor of OMT (Gundermann 2013, Hensel et al 2015, Licciardone et al 2010, Peters & van der Linde 2006), 2 comparisons had non-significant effects in favor of OMT (Licciardone &
Aryal 2013, Röhrich 2014), and 1 comparison had non-significant effects in favor of
the control (Hensel et al 2015). There was moderate quality evidence (downgraded
due to inconsistency) that OMT had a significant medium-sized effect on decreasing
pain (MD, -16.75; 95% CI, -31.79 to -1.72) and increasing functional status (SMD, -
0.50; 95% CI, -0.93 to -0.07) in women with LBP during pregnancy (Figures 1 & 2).

OMT for low back and posterior pelvic pain after pregnancy (postpartum)
Three studies (Belz 2014, Recknagel & Roß 2007, Schwerla et al 2015) with 3
comparisons and 180 participants were analysed for effect of OMT on postpartum low
back and pelvic girdle pain. The 3 studies each reported significant effects in favor of
OMT for pain and for functional status. There was low-quality evidence (downgraded
due to imprecision and inconsistency) that OMT had a significant large-sized effect
on decreasing pain (MD, -38.00; 95% CI, -46.75 to -29.24) and increasing functional
status (SMD, -2.12; 95% CI, -3.02 to -1.22) in women with postpartum LBP (Figures
3 & 4).

Subgroup analysis
Regarding OMT for LBP in pregnancy, subgroup analysis to examine OMT versus
each specific intervention all suffered from high heterogeneity and imprecision (too
few participants). Significant effects in favour of OMT were found with untreated
control groups (Gundermann 2013, Peters & van der Linde 2006, Röhrich 2014) for
pain (MD, -36.11; 95% CI, -49.17 to -23.05) and function (SMD, -0.98; 95% CI, -
1.45 to -0.52), but no significant effects were found when the comparison was sham
control (Hensel et al 2015, Licciardone et al 2010) (pain: MD, -2.47; 95% CI, -4.60 to
10.08; function: SMD, -0.11; 95% CI, -0.35 to 0.58). In comparisons where only a
single study was available, such as OMT versus usual care (Hensel et al 2015) and
OMT plus usual care versus usual care alone (Licciardone et al 2010), a significant
effect was evident in favour of OMT.
The subgroup analyses to determine if there were differences in effects of the published and unpublished studies also all suffered from high heterogeneity and imprecision (too few participants). Regarding OMT for LBP during pregnancy, there were significant effects in the unpublished studies (Gundermann 2013, Peters & van der Linde 2006, Röhrich 2014) for pain (MD, -36.11; 95% CI, -49.17 to -23.05) and function (SMD, -0.98; 95% CI, -1.45 to -0.52), but not in the published studies (Hensel et al 2015, Licciardone et al 2010). Regarding OMT for postpartum LBP, there were significant effects in the unpublished studies (Belz 2014, Recknagel & Roß 2007) for pain (MD, -33.37; 95% CI, -40.30 to -26.43) and function (SMD, -1.67; 95% CI, -2.15 to -1.19) as well as in the single published study (Schwerla et al 2015) for pain (MD, -44.70; 95% CI, -50.94 to -38.46) and function (SMD, -3.02; 95% CI, -3.67 to -2.37).

Adverse events
Schwerla et al. (Schwerla et al 2015) noted that no serious adverse events were reported by patients, although some patients occasionally reported being tired after treatment. No other study reported on adverse events from treatment. In personal communications, the authors of 2 other studies (Belz 2014, Gundermann 2013) reported that no adverse events occurred.

DISCUSSION
The current review found that OMT significantly improved both pain and function in women with low back and pelvic pain during pregnancy. It also found that OMT significantly improved both pain and function in women with postpartum low back and pelvic pain. The size of the effects was medium and were clinically relevant (Furlan et al 2009). All studies were considered to have low risk of bias. Only 1 of the studies specifically reported on adverse effects of treatment, which were reported as being minor.

This review updated the analysis of OMT for women with low back and pelvic pain during pregnancy and postpartum from the review of Franke et al. (Franke et al 2014). For pain during pregnancy, the current review included an additional 2 studies (Hensel et al 2015, Röhrich 2014), adding a further 3 comparisons and 435 participants to the analysis. The current review found a medium effect of treatment for
pain, whereas the previous review found a large effect (Franke et al 2014). For functional status during pregnancy, the current review found a medium effect of OMT, which was consistent with the previous review. Given the additional studies and larger participant numbers, the medium effects of the current review are more credible. Further, the quality of the evidence according to the GRADE approach has also improved from low to moderate in the current review.

The current review included 3 studies of OMT for women with postpartum pain. It updated the previous review (Franke et al 2014) with an additional study (Belz 2014), but the number of participants for this comparison was still small at 173. The current review found a large effect in pain and functional status in postpartum women, which was consistent with the previous review. However, the quality of the evidence as assessed using GRADE was low due to imprecision from low participant numbers and inconsistency due to heterogeneity in the analysis. The additional study (Belz 2014) in the current review increased the statistical heterogeneity and resulted in a reduction in the level of quality of this analysis compared to the previous review (Franke et al 2014).

There is a lack of high-quality evidence for effective treatment of low back and pelvic pain in women during and after pregnancy. In a systematic review, Liddle and Pennick (Liddle & Pennick 2015) reported that there was low-quality evidence that exercise may reduce pregnancy-related LBP and moderate- to low-quality evidence suggesting that any exercise improves functional disability. No specific form of exercise appeared to be more effective and both land and water exercises with usual prenatal care were compared to usual prenatal care only. Similar to the effects of OMT in the current review, medium effect sizes were reported for the effect of exercise. The quality of the evidence was low due to study design limitations and inconsistency of results (Liddle & Pennick 2015). Inconsistency of results was a limitation also encountered in the current review and common to reviews of studies with small sample sizes. Liddle and Pennick (Liddle & Pennick 2015) also reported that there was low-quality evidence from single studies suggesting the possible effectiveness of a variety of other treatments, such as OMT, water gymnastics, a supervised progressive muscle relaxation programme with music, craniosacral therapy, a non-rigid lumbopelvic belt, and acupuncture. Comparisons of the
effectiveness of these treatments with OMT are difficult because of the low-quality evidence for most interventions, the fact that new research is very likely to change the estimate of effect, and the comparison interventions were different in different studies. If future studies use more standardized comparisons, such as usual medical care, comparisons between different interventions will be possible.

While the current study found moderate quality evidence that OMT benefits LBP pain during pregnancy and low evidence for postpartum pain, the mechanisms for therapeutic effect are unclear. OMT is commonly advocated for improving motion and biomechanical function (DeStefano 2012, DiGiovanna et al 2005), and while there is limited evidence supporting short-term increases in motion following OMT (Clements et al 2001, Fryer & Ruszkowski 2004, Lau et al 2011, Millan et al 2012, Schenk et al 1994, Schenk et al 1997), it seems unlikely that this is an important mechanism in this population given that ligamentous laxity and lack of stability may be underlying factors (Gutke et al 2008a, Majchrzycki et al 2010, Vermani et al 2010, Vleeming et al 2008). The hypoalgesic effects of a variety of manual techniques are well reported and have been demonstrated to reduce pain and pressure pain sensitivity, at least in the short-term (Aguirrebena et al 2016, Bervoets et al 2015, Coronado et al 2012, Nunes et al 2016). It is likely that pain modulation from manual techniques occurs mainly by neurophysiological mechanisms (Bialosky et al 2009, Vigotsky & Bruhns 2015). It may be possible that improvements in pain from manual therapy leads to better neuromuscular function and control, improved psychological outlook and pain coping strategies, and overall wellness. However, the mechanisms underlying improvement in pain and function from OMT require further investigation.

All studies used treatment approaches that included a wide range of osteopathic techniques (DeStefano 2012, DiGiovanna et al 2005): ‘structural’ techniques, such as soft tissue manipulation, stretching, joint mobilisation, muscle energy technique, and spinal manipulation, as well as visceral and cranial techniques. The treatments typically addressed palpated dysfunctions not just in the low back region, but the whole body. Although the range of different osteopathic techniques used in each study was similar, it is not possible to know how comparable the treatments from different studies were because of lack of detail in the descriptions of treatments, and it is possible that the emphasis on techniques was different between studies.
To our knowledge, this review is the most comprehensive for the treatment of LBP with OMT in women during and after pregnancy. It updated a previous review by the addition of several new studies on this topic (Belz 2014, Hensel et al 2015, Röhrich 2014). The current review was not restricted to the English language or to published studies. Six of the included studies were from Germany (Gundermann 2013, Peters & van der Linde 2006, Recknagel & Roß 2007, Röhrich 2014, Schwerla et al 2015) and 2 were from the United States (Hensel et al 2015, Licciardone et al 2010). The large number from Germany was surprising, but probably represents the particular requirements of research for post-graduate study of osteopathy in that country and that research is seen as important for professional recognition. Of the 6 German studies, only 1 was published in the peer-reviewed literature (Schwerla et al 2015). The other 5 studies were unpublished research theses (Gundermann 2013, Peters & van der Linde 2006, Recknagel & Roß 2007, Röhrich 2014). Searching the unpublished grey literature for relevant studies is recommended by the Cochrane Collaboration for a more comprehensive search and to avoid publication bias (Higgins & Green 2011).

The subgroup analysis investigating differences between published and unpublished studies showed no difference between the 2 for postpartum LBP, but there were significant effects in the unpublished studies (Gundermann 2013, Peters & van der Linde 2006, Röhrich 2014), but not in the published studies (Hensel et al 2015, Licciardone et al 2010), of OMT for LBP during pregnancy. The reasons for this difference are unclear. All included studies were judged to have low risk of bias. However, the unpublished studies typically had a smaller sample size, and smaller studies tend to produce larger effect sizes (Dechartres et al 2013). The studies with the largest samples were the 2 studies from the United States (Hensel et al 2015, Licciardone et al 2010), which may relate to the funds available for osteopathic research in the United States. While the total number of included studies is still small, LBP in women during and after pregnancy is a clinical problem where few modalities have been well researched (Liddle & Pennick 2015). This review adds to the sparse literature in this field.

The conclusions of the current review are limited by the small number of available studies and low sample sizes of many of these studies. Small studies are more likely
to produce variation and inconsistency of results, and statistical heterogeneity was found in all the meta-analyses. These limitations are reflected by the downgrading of the level of evidence for OMT in both pregnancy and postpartum pain due to inconsistency (statistical heterogeneity) and due to imprecision (sample smaller than 400 participants) in the analysis of postpartum pain. Given the moderate level of evidence for pain in pregnancy and low level of evidence for pain in postpartum, further research is likely to have an important impact on our estimate of effect of OMT, particularly for pain during postpartum.

Additionally, the conclusions of the current review are limited by the different comparison groups and the lack of long-term follow-up. For LBP during pregnancy, the comparison interventions included usual obstetric care (Hensel et al 2015, Licciardone et al 2010), sham ultrasound (Hensel et al 2015, Licciardone et al 2010), and no treatment (Gundermann 2013, Peters & van der Linde 2006, Röhrich 2014). Although the subgroup analysis cannot be considered robust because of the lack of studies, heterogeneity, and imprecision, it appeared that the different comparisons produced different effects and may contribute to the statistical heterogeneity in the main analysis. For LBP postpartum, the comparison group was untreated (Belz 2014, Recknagel & Roß 2007, Schwerla et al 2015). It is possible that usual care would produce different effects to no treatment and this should be considered when making recommendations about treatment. The lack of long-term follow-up by studies in this review is also cause for caution when making recommendations.

Given the moderate and low levels of evidence and the likely impact of further research, more studies on these research questions are needed, in particular, high-quality studies with large sample sizes, robust comparisons, and adequate follow-up. Only 1 study reported the presence or absence of adverse events, so future studies should make a statement on adverse events and adhere to recommended reporting guidelines (Schulz et al 2010).

**CONCLUSIONS**

The current review updated a previous review (Franke et al 2014) on the effectiveness of OMT for pregnancy-related LBP. We found moderate-quality evidence that OMT had a significant medium-sized effect on decreasing pain and increasing functional
status in women with LBP during pregnancy and low-quality evidence that OMT had a significant large-sized effect on decreasing pain and increasing functional status for postpartum LBP. Our results suggest that OMT may produce clinically relevant benefits for women with these conditions. Given the small sample sizes, different comparison groups, statistical heterogeneity, and lack of long-term follow-up, large high-quality RCTs are still needed to provide more confident conclusions regarding the effectiveness of OMT for LBP in women during pregnancy and postpartum.
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Saurel-Cubizolles MJ, Romito P, Lelong N, Ancel PY 2000 Women's health after childbirth: a longitudinal study in France and Italy. BJOG 107: 1202-1209


Schenk RJ, MacDiarmid A, Rousselle J 1997 The effects of muscle energy technique on lumbar range of motion. J Man Manip Ther 5: 179-183


**Table 1.** Search Terms and Strategy Used for MEDLINE

1. randomized controlled trial[Publication Type]
2. controlled clinical trial[Publication Type]
3. randomized[Title/Abstract]
4. placebo[Title/Abstract]
5. randomly[Title/Abstract]
6. trial[Title/Abstract]
7. groups[Title/Abstract]
8. or/1-7
9. (animals NOT (humans and animals)) MeSH Subheading
10. 8 not 9
11. dorsalgia[Title/Abstract]
12. back pain[Title/Abstract]
13. backache[Title/Abstract]
14. lumbar adj pain AND Title/Abstract
15. coccyx[Title/Abstract]
16. coccydynia[Title/Abstract]
17. sciatica[Title/Abstract]
18. sciatic neuropathy[Title/Abstract]
19. spondylosis[Title/Abstract]
20. lumbago[Title/Abstract]
21. low back pain[Title/Abstract]
22. lumbopelvic pain[Title/Abstract]
23. or/11-22
24. 10 and 23
25. osteopathic medicine[MeSH Terms]
26. manipulation, osteopathic[MeSH Terms]
27. OMT[Title/Abstract]
28. or/25-27
29. "Pregnancy"[Mesh]
30. "Postpartum Period"[Mesh]
31. or/29-30
32. 24 and 28 and 31
Table 2. Overview of Included Clinical Trials for Osteopathic Manipulative Treatment for Women with Low Back Pain During and After Pregnancy

<table>
<thead>
<tr>
<th>Author and year</th>
<th>Country</th>
<th>Study design</th>
<th>Aim of the study</th>
<th>Duration of pain</th>
<th>Reported inclusion/ exclusion criteria</th>
<th>Outcome measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gundermann 2013</td>
<td>Germany</td>
<td>RCT</td>
<td>To evaluate the effectiveness of osteopathic treatment in pregnant women suffering from LBP</td>
<td>At least 1 week</td>
<td>+/-</td>
<td>1. VAS, 2. Frequency of pain, 3. RMDQ, 4. Questionnaire postpartum</td>
</tr>
<tr>
<td>Hensel 2015</td>
<td>USA</td>
<td>RCT</td>
<td>To evaluate the efficacy of OMT to reduce LBP and improve functioning during the third trimester in pregnancy and to improve selected outcomes of labor and delivery</td>
<td>Not specified</td>
<td>+/</td>
<td>1. QVAS, 2. RMDQ, 3. Labor and delivery records</td>
</tr>
<tr>
<td>Licciardone 2010</td>
<td>USA</td>
<td>RCT</td>
<td>Examination of OMT for back pain and related symptoms during the third trimester of pregnancy</td>
<td>Not specified</td>
<td>+/-</td>
<td>1. Back pain on an 11-point scale, analyzed like a 10-cm VAS for pain, 2. RMDQ</td>
</tr>
<tr>
<td>Peters 2006</td>
<td>Germany</td>
<td>RCT</td>
<td>Assessing whether OMT influences the pain symptomatology of women with pregnancy-related LBP</td>
<td>At least 1 week</td>
<td>+/-</td>
<td>1. VAS, 2. Quebec Back Pain Disability Scale</td>
</tr>
<tr>
<td>Röhrich 2014</td>
<td>Germany</td>
<td>RCT</td>
<td>To evaluate the effectiveness of osteopathic treatment in pregnant women suffering from LBP</td>
<td>At least 1 week</td>
<td>+/-</td>
<td>1. VAS, 2. Frequency of pain, 3. Disability in daily activities with RMDQ, 4. Frequency of osteopathic dysfunctions</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No. of patients (randomized)/ dropouts</th>
<th>No. of patients/ mean age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a = 21/ 29 years</td>
</tr>
<tr>
<td></td>
<td>b = 20/ 31 years</td>
</tr>
<tr>
<td></td>
<td>a = 136/ 23.0 years</td>
</tr>
<tr>
<td></td>
<td>b = 131/ 24.1 years</td>
</tr>
<tr>
<td></td>
<td>c = 133/ 24.70 years</td>
</tr>
<tr>
<td></td>
<td>a = 49/ 23.8 years</td>
</tr>
<tr>
<td></td>
<td>b = 48/ 23.7 years</td>
</tr>
<tr>
<td></td>
<td>c = 49/ 23.8 years</td>
</tr>
<tr>
<td></td>
<td>a = 30/ 30.6 years</td>
</tr>
<tr>
<td></td>
<td>b = 30/ 30.2 years</td>
</tr>
<tr>
<td></td>
<td>a = 17/ 32.7 years</td>
</tr>
<tr>
<td></td>
<td>b = 18/ 30.3 years</td>
</tr>
</tbody>
</table>
### Treatment (No.)

<table>
<thead>
<tr>
<th>a. Intervention</th>
<th>b. Control</th>
<th>c. Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>a = OMT (4)</td>
<td>a = OMT (7)</td>
<td>a = UOBC + OMT (7)</td>
</tr>
<tr>
<td>b = untreated</td>
<td>b = SUT</td>
<td>b = UOBC</td>
</tr>
<tr>
<td>c = UC</td>
<td>c = UOBC</td>
<td></td>
</tr>
</tbody>
</table>

### Author conclusions

Four osteopathic treatments led to significant and clinically relevant positive changes in pain intensity and frequency in pregnant women suffering from LBP.

OMT was effective for mitigating pain and functional deterioration compared with UC but did not differ significantly from SUT.

OMT slows or halts the deterioration of back-specific functioning during the third trimester of pregnancy.

Four osteopathic treatments caused a clinically relevant influence on pain and the interference of daily life for pregnant women with pain in the pelvic and/or lumbar area.

### Postpartum Studies

<table>
<thead>
<tr>
<th>Author and year</th>
<th>Country</th>
<th>Study design</th>
<th>Aim of the study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belz 2014</td>
<td>Germany</td>
<td>RCT</td>
<td>To evaluate the effectiveness of custom-tailored osteopathic treatment in women suffering from persistent non-specific LBP after childbirth</td>
</tr>
<tr>
<td>Recknagel 2007</td>
<td>Germany</td>
<td>RCT</td>
<td>Investigation of whether OMT had an effect on women with postpartum persistent unspecific backache</td>
</tr>
<tr>
<td>Schwerla 2015</td>
<td>Germany</td>
<td>RCT</td>
<td>To evaluate the effectiveness of osteopathic treatment in women suffering from persistent LBP after childbirth</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Duration of pain</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>At least 3 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At least 3 months, not more than 24 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After childbirth for at least 3 months and at most 20 months</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reported inclusion/exclusion criteria</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>+/-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>+/</td>
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<td></td>
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<tr>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome measurement</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. VAS, 2. Frequency of pain, 3. Effect of LBP on everyday activities with PGPQ, 4. Frequency of osteopathic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. VAS, 2. PGPQ, 3. Regions of dysfunction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. VAS, 2. OPQ, 3. Different specific health problems</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>dysfunctions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------</td>
<td>--------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>No. of patients</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(randomized)/ dropouts</td>
<td>60/ 6</td>
<td>40/ 1</td>
<td>80/ 3</td>
</tr>
<tr>
<td><strong>No. of patients/ mean age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Intervention</td>
<td>a = 30/ 33.8 years</td>
<td>a = 20/ 34.5 years</td>
<td>a = 39/ 33.9 years</td>
</tr>
<tr>
<td>b. Control</td>
<td>b = 30/ 34.3 years</td>
<td>b = 19/ 34.4 years</td>
<td>b = 40/ 33.3 years</td>
</tr>
<tr>
<td>c. Control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Treatment (No.)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Intervention</td>
<td>a = OMT (5)(^1)</td>
<td>a = OMT (4)</td>
<td>a = OMT (4)</td>
</tr>
<tr>
<td>b. Control</td>
<td>b = untreated</td>
<td>b = no treatment</td>
<td>b = untreated</td>
</tr>
<tr>
<td>c. Control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Author conclusions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Five osteopathic treatments over a period of 10 weeks led to significant and clinically relevant positive changes to pain intensity and everyday activities in women suffering from persistent non-specific LBP after childbirth.</td>
<td>OMT brings about clinically relevant improvement of pain and a reduction of the impediment on daily life for women with persistent, unspecific backache postpartum.</td>
<td>Four osteopathic treatments over a period of 8 weeks led to significant and clinically relevant positive changes of pain intensity and everyday activities in women suffering from LBP after childbirth.</td>
</tr>
</tbody>
</table>

\(^1\)The outcome measurement of the 5th treatment was incorrectly reported; the measurements after 4 treatments were used for analysis.

Abbreviations: LBP, low back pain; NRS, Numeric Rating Scale; OMT, osteopathic manipulative treatment; OPQ, Oswestry Pain Questionnaire; PGPQ, Pelvic Girdle Pain Questionnaire; QVAS, Quadruple Visual Analogue Scale; RCT, randomized controlled trial; RMDQ, Roland Morris Disability Questionnaire; SUT, sham ultrasound treatment; UC, usual care; UOBC, usual obstetric care; VAS, visual analogue scale pain.
Table 3. Risk of Bias in the Included Studies

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Belz 2014</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>HR</td>
<td>HR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
</tr>
<tr>
<td>Gundermann 2013</td>
<td>LR</td>
<td>LR</td>
<td>HR</td>
<td>HR</td>
<td>HR</td>
<td>HR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
</tr>
<tr>
<td>Hensel 2015</td>
<td>LR</td>
<td>LR</td>
<td>HR</td>
<td>HR</td>
<td>HR</td>
<td>HR</td>
<td>LR</td>
<td>LR</td>
<td>HR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
</tr>
<tr>
<td>Licciardone 2010</td>
<td>LR</td>
<td>UC</td>
<td>HR</td>
<td>HR</td>
<td>HR</td>
<td>HR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
</tr>
<tr>
<td>Peters 2006</td>
<td>LR</td>
<td>LR</td>
<td>HR</td>
<td>HR</td>
<td>HR</td>
<td>HR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
</tr>
<tr>
<td>Recknagel 2007</td>
<td>LR</td>
<td>LR</td>
<td>HR</td>
<td>HR</td>
<td>HR</td>
<td>HR</td>
<td>HR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
</tr>
<tr>
<td>Röhrich 2014</td>
<td>LR</td>
<td>LR</td>
<td>HR</td>
<td>HR</td>
<td>HR</td>
<td>HR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
</tr>
<tr>
<td>Schwerla 2015</td>
<td>LR</td>
<td>LR</td>
<td>HR</td>
<td>HR</td>
<td>HR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
<td>LR</td>
</tr>
</tbody>
</table>

1 In manual therapy studies, blinding is not possible.
2 For patient-reported outcomes, a low risk of bias is only possible if there is a low risk of bias for participant blinding.
Abbreviations: HR, high risk of bias; LR, low risk of bias; UC, unclear.
**Table 4. OMT Compared to Usual Obstetric Care, Sham Ultrasound, and Untreated for Nonspecific Low Back Pain in Pregnancy**

**Patient or population:** patients with nonspecific low back pain in pregnancy  
**Intervention:** OMT  
**Comparison:** usual obstetric care, sham ultrasound, and untreated

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No. of participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Assumed risk</td>
<td>Corresponding risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Usual obstetric care, sham ultrasound and untreated</strong></td>
<td>OMT</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pain</strong></td>
<td>The mean pain in the intervention groups was</td>
<td></td>
<td>725 (5 studies)</td>
<td>⚫⚫⚫⚫ (moderate)</td>
</tr>
<tr>
<td>Visual Analogue Scale from 0 to 100 (worst pain)</td>
<td>16.65 lower (31.12 to 2.17 lower)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Functional status</strong></td>
<td>The mean functional status in the intervention groups was</td>
<td></td>
<td>725 (5 studies)</td>
<td>⚫⚫⚫⚫ (moderate)</td>
</tr>
<tr>
<td>Roland Morris Disability Questionnaire, Quebec Back Pain Disability Scale</td>
<td>0.50 standard deviations lower (0.93 to 0.07 lower)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The basis for the assumed risk (e.g., the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% CI) is
based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

**CI**: Confidence interval.

**GRADE Working Group grades of evidence**

**High quality**: Further research is very unlikely to change our confidence in the estimate of effect.

**Moderate quality**: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

**Low quality**: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

**Very low quality**: We are very uncertain about the estimate.

1 $I^2=94$

2 $I^2=84$

15

16
Table 5. OMT Compared to Untreated for Nonspecific Low Back Pain Postpartum

**Patient or population**: patients with nonspecific low back pain postpartum

**Intervention**: OMT

**Comparison**: untreated

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No. of participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pain</strong></td>
<td>The mean pain in the intervention groups was <strong>38.00 lower</strong> (46.75 to 29.24 lower)</td>
<td></td>
<td>173</td>
<td>⊕⊕⊕⊕ low^1^</td>
</tr>
<tr>
<td>Visual Analogue Scale from 0 to 100 (worst pain)</td>
<td></td>
<td></td>
<td>(3 studies)</td>
<td></td>
</tr>
<tr>
<td><strong>Functional status</strong></td>
<td>The mean functional status in the intervention groups was <strong>2.12 standard deviations lower</strong> (3.02 to 1.22 lower)</td>
<td></td>
<td>173</td>
<td>⊕⊕⊕⊕ low^2^</td>
</tr>
<tr>
<td>Roland Morris Disability Questionnaire, Pelvic Girdle Pain Questionnaire</td>
<td></td>
<td></td>
<td>(3 studies)</td>
<td></td>
</tr>
</tbody>
</table>

*The basis for the **assumed risk** (e.g., the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

\(^1\) I^2 = 68\%

\(^2\) Sample size < 400

\(^3\) I^2 = 81\%
FIGURES

**Figure 1.** Osteopathic Manipulative Treatment (OMT) for Nonspecific Low Back Pain During Pregnancy. Outcome: Pain
Abbreviations: CI, confidence interval; SD, standard deviation.

**Figure 2.** Osteopathic Manipulative Treatment (OMT) for Nonspecific Low Back Pain During Pregnancy. Outcome: Functional Status
Abbreviations: CI, confidence interval; SD, standard deviation.

**Figure 3.** Osteopathic Manipulative Treatment (OMT) for Nonspecific Low Back Pain Postpartum. Outcome: Pain
Abbreviations: CI, confidence interval; SD, standard deviation.

**Figure 4.** Osteopathic Manipulative Treatment (OMT) for Nonspecific Low Back Pain Postpartum. Outcome: Functional Status
Abbreviations: CI, confidence interval; SD, standard deviation.
Figure 1. OMT for nonspecific low back pain during pregnancy. Outcome: Pain
Figure 2. OMT for nonspecific low back pain during pregnancy. Outcome: Functional status
Figure 3. OMT for nonspecific low back pain postpartum. Outcome: Pain
Figure 4. OMT for nonspecific low back pain postpartum. Outcome: Functional status

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>OMT Mean</th>
<th>OMT SD</th>
<th>OMT Total</th>
<th>Control Mean</th>
<th>Control SD</th>
<th>Control Total</th>
<th>Weight</th>
<th>Std. Mean Difference IV Random, 95% CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rechnagle 2007</td>
<td>10.7</td>
<td>12.1</td>
<td>20</td>
<td>23.0</td>
<td>19.3</td>
<td>19</td>
<td>32.2%</td>
<td>-1.51 [-2.31, -0.81] 2007</td>
</tr>
<tr>
<td>Belz 2014</td>
<td>9.2</td>
<td>9.1</td>
<td>27</td>
<td>22</td>
<td>18.4</td>
<td>27</td>
<td>34.0%</td>
<td>-1.74 [-2.37, -1.11] 2014</td>
</tr>
<tr>
<td>Schwenke 2015</td>
<td>2.08</td>
<td>1.54</td>
<td>40</td>
<td>10</td>
<td>3.34</td>
<td>40</td>
<td>33.7%</td>
<td>-3.02 [-3.67, -2.37] 2015</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>0.7</td>
<td>0.6</td>
<td>87</td>
<td>86</td>
<td>100.0%</td>
<td></td>
<td></td>
<td><strong>-2.12 [-3.02, -1.22]</strong></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.51; Chi² = 10.78, df = 2 (P = 0.005); I² = 81%

Test for overall effect: Z = 4.03 (P < 0.0001)