

# Systematic review of spinal manipulation in children under 12 years

Update of 2019 systematic review for Safer Care Victoria

Report prepared by Cochrane Australia for the Australian Health Practitioner Regulation Agency (AHPRA)

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# **Executive Summary**

The Australian Health Practitioner Regulation Agency (AHPRA) commissioned Cochrane Australia to update a systematic review of the effectiveness and safety of spinal manipulation (SMT) in children under 12 years, conducted for Safer Care Victoria in 2019. The original review included 13 studies of the effectiveness of SMT and 10 studies relating to safety.

For this update we searched PubMed, Cochrane Central Register of Controlled Trials, Embase, AMED, Emcare, CINAHL and Scopus on 20 October 2022 for studies of spinal manipulation published since June 2019. We included two randomised trials of the effectiveness of spinal manipulation (headache and ADHD) and one case report of a severe adverse effect.

When combined with a randomised trial of headache included in the 2019 review, we found low certainty evidence that spinal manipulation compared with sham SMT may reduce the mean number of days per week with headache (0.37 days per week fewer, 95% CI 0.72 days to 0.02 days per week fewer; 2 trials; 245 children). However, the confidence interval is compatible with both a small potentially important reduction and little or no difference. We found moderate certainty evidence that SMT probably results in little or no difference in headache pain intensity (0.22 points lower, 95% CI 0.62 points lower to 0.19 points higher on a 10-point scale; 2 trials; 222 children).

We found very low certainty evidence that total reading time per sentence was shortened among children with ADHD who received spinal manipulation compared with a control (0.07 fewer seconds, 95% CI 1.08 fewer seconds to 0.94 more seconds; 1 trial; 47 children). However, the confidence interval is very wide and includes both a decrease and an increase in reading time.

One case report of an adverse effect was classified as severe and involved an 8-year-old girl who received cervical manipulation from a massage therapist for relief of asthma. The girl developed intense neck pain and received treatment in hospital for atlantoaxial rotatory subluxation. The patient was placed in a cervical orthosis for 6 weeks and made a full recovery with relief of pain and maintenance of neck full range of motion.

Overall, the findings of this update do not alter the conclusions reached in the original review that "due to the paucity of studies and the lack of reported information on the specific treatment techniques employed, it is difficult to draw conclusions about the safety and effectiveness of spinal manipulation in children."

# **Objectives**

To identify any new evidence relating to both the effectiveness and safety of spinal manipulation in children under 12 years of age.

# Eligibility criteria

To assess the effectiveness and safety of **spinal manipulation**, defined as any technique delivered by any health professional that involves a high velocity, low amplitude thrust beyond the physiological range of motion, impacting the spine, within the limits of anatomical integrity, conducted in **children under 12 years** for **any condition or symptoms**.

For the effectiveness review, eligible studies included both randomised trials and observational studies, provided the observational studies included a comparator (e.g., non-randomised trial, cohort study, controlled before-and-after study). Exclusions included non-comparative studies (e.g., case reports or case series without pre and post measurements or a control group) and cross-sectional studies.

For the safety review any article reporting adverse events was eligible, irrespective of the study type (i.e., trials, observational studies, case reports, etc.). Articles not reporting case information (e.g., commentaries or editorials) were excluded, as were full-text reports not available in English.

## Methods

#### Identification of studies

We searched PubMed, Cochrane Central Register of Controlled Trials (CENTRAL via Cochrane Library), Embase, Allied and Complementary Medicine (AMED), Emcare, CINAHL, and Scopus. The MeSH terms included in the PubMed search were translated into the appropriate subject headings for each database. See Appendix 8 for the search strategies.

All searches were run on 20 October 2022 and were not restricted by language or format of publication. The PubMed search was restricted to records added from June 2019 (the date searches were run for the 2019 review). For all other databases searches were limited to publication year 2019 onwards. Since the search was not limited by study design, studies of effectiveness and safety were retrieved using the same search strategies.

The reference lists of eligible studies and relevant systematic reviews were checked for additional studies.

#### Selection of studies

Records from the database searches were first imported to EndNote and duplicates removed, and then imported to Covidence for screening. The titles and abstracts were single screened (Steve McDonald), with only the obviously irrelevant records being excluded at this stage. The full-text of all potentially eligible studies were retrieved and single-screened (by SM) in the first instance.

Editorials, commentaries, etc. were excluded and systematic reviews set aside for further assessment. Potentially eligible primary studies of the effectiveness of spinal manipulation and reports relating to safety of spinal manipulation were screened by two people (SM and Sally Green). Studies were excluded based on participant age, intervention or study design. The final decision on the inclusion of studies was agreed by consensus.

#### Systematic reviews

Systematic reviews and overviews that overlapped with the scope of this review were identified during the screening phase and the list of included studies (effectiveness and safety) were cross-checked against the 2019 review. Given the large number of systematic reviews we retrieved, generally only reviews that had a search date more recent than May 2019 were assessed for additional studies.

#### Data extraction and risk of bias assessment

Study characteristics and data were extracted by one reviewer (Melissa Murano) and checked by a second (SM). The Cochrane RoB 2 tool was used to assess risk of bias, with judgements made by one reviewer (MM) and checked by a second (SM).

#### Synthesis and GRADE assessment

We conducted meta-analysis where this was feasible and appropriate. The overall certainty of the evidence was assessed for each condition/outcome using GRADE criteria where feasible (risk of bias, consistency, imprecision, indirectness and publication bias) and the evidence rated as high, moderate, low or very low. We updated the original summary of findings tables (prepared using the GRADEpro GDT software) with new studies.

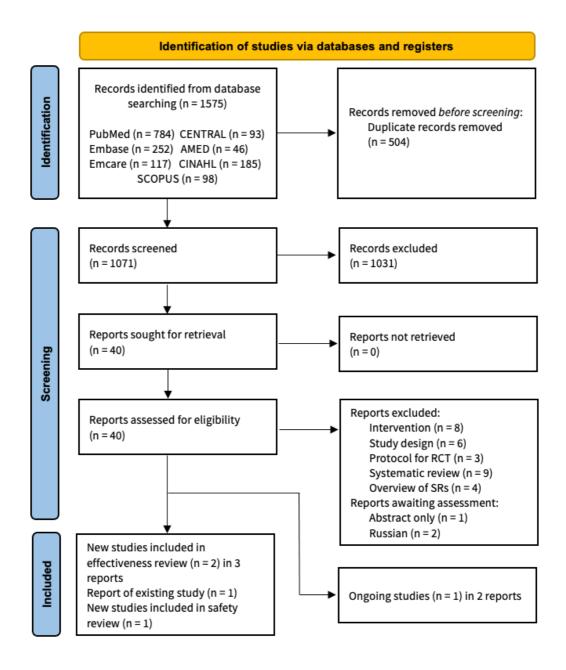
#### Results

#### Results of search

The search retrieved 1071 unique records (after 504 duplicates were removed). 1031 records were excluded at the title/abstract stage, leaving the full text of 40 reports to assess for eligibility.

We excluded 15 primary studies of effectiveness published since 2019, plus two from pre-2019 (Appendix 4). We also excluded one primary study of safety (Appendix 5). Three studies (one conference abstract; two papers published in Russian) are listed as awaiting assessment as it is unclear (though unlikely) if the intervention meets the criteria for HVLA (Appendix 5). Thirteen systematic reviews and overviews were excluded, having first checked whether they included any new additional primary studies (Appendix 6 and 7).

Two new effectiveness studies met the inclusion criteria, along with one follow-up report to an existing study. One study is only available as a conference abstract and is listed as ongoing. One safety study was identified. (See Appendix 1 and PRISMA flow diagram below.)



#### Summary of included studies

Two new studies of effectiveness were identified (30 children with ADHD (Cade 2021); 199 children with headache (Lynge 2021)). The study characteristics of Cade 2021 and Lynge 2021 are given in Table 1.

One study of 269 children with autism spectrum disorder (Voloshyn 2022) is only available as a conference abstract and has limited usable data. The results, as presented in the abstract, are given in Appendix 1. Due to sparse data and insufficient information about its conduct, this study is categorised as ongoing, and no further analysis has been undertaken.

We also identified a secondary analysis of a randomised trial included in the 2019 review (Dissing 2019; 238 children with back/neck pain).

The only safety study we identified was a case report of an 8-year-old female with asthma who suffered atlantoaxial rotatory subluxation following cervical manipulation by a massage therapist (Pedro 2020) (Table 2 and Appendix 2).

#### Risk of bias assessment

Cade 2021 (ADHD) was considered to be at high risk of bias due to potential carryover effects evident with the crossover design and incomplete data due to equipment calibration issues. Lynge 2021 (headache) was considered to be at low risk of bias. (See Table 3.)

Table 1. Characteristics of included studies – effectiveness

Condition	Study ID / Country Practitioner/ Setting	Study objective	Study design / Sample size	Patient description (age) and condition	Description of intervention and comparator	Outcome(s) measured (main bolded)	Result for main outcome (conclusion if result not reported)	Adverse events
Attention deficit hyperactivity disorder (ADHD)	Cade 2021 New Zealand Chiropractor NZ College of Chiropractic or participants' homes	To evaluate efficacy of spinal manipulation on oculomotor control in children with ADHD	Crossover RCT (1- week washout) Feasibility study n = 30	Children aged 8– 15 years (57% 8– 11 years) with parent-reported diagnosis of ADHD	Single session of chiropractic spinal and/or pelvic manipulation (HVLA thrusts) vs passive & active movements of head, spine and body (active control)	Oculomotor control as measured by target acquisition time, no. of distractors, reading time, number, time and length of forward and reverse fixations and saccades (immediate post-treatment, target acquisition and reading)	Improvements in reading time post SMT compared to post active control. Lower active control baseline reading times for participants receiving SMT first suggest carryover effects (insufficient wash-out period) and/or effect of baseline characteristic differences.	Not mentioned
Headache	Lynge 2021 Denmark Chiropractor Private practices (chiropractic or paediatric)	To evaluate the efficacy of spinal manipulation in children with recurrent headaches	RCT n = 199	Children aged 7– 14 years (mean age 10.8 years) with recurrent headaches (min. 1 per week for at least 6 months) and min. 1 musculoskeletal dysfunction in spine, pelvis and/or temporomandibular joint	Chiropractic manipulative therapy (CMT) (HVLA thrust) of spine, pelvis and/or temporomandibula r joints vs sham manipulation (both groups received advice and usual care, incl. medication as needed)	No. of days with headache, average pain intensity assessed via weekly SMS (change in average values during 4-week pretreatment period and final 4 weeks of study period (weeks 14–17)). Other: global perceived effect, medication	Days per week with headaches were reduced by 0.81 days for CMT compared with 0.41 days for sham (MD -0.40, 95% CI -0.77 to -0.03). There was no difference in average pain intensity change scores (MD 0.01; 95% CI: -0.43 to 0.46) between the groups.	84% in CMT and 75% in sham group reported mild side effects of short duration after at least one consultation. No serious side effects.

Table 2. Characteristics of included studies – safety

Study ID / Country Practitioner/ Setting	Study design/ Sample size	Key findings	No. of adverse events	Description of adverse event	Description of patient(s)/ Presenting condition	Description of technique	Underlying pathology	Notes on method
Pedro 2020 Philippines Massage therapist Setting unknown	Case report n = 1	N/A	1	Atlantoaxial rotatory subluxation (AARS)	8-year-old female with asthma	Aggressive manipulation of the neck repeated rotatory/ twisting motions and digital pressure over joints of spine.	Nil	Qualifications or experience of the therapist not stated.

Table 3. Risk of bias summary

Author/ year	Condition sample size (n) / Primary outcome	Randomisation process	Period & carryover effects bias (crossover trials)	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall risk of bias
Cade 2021	ADHD (n = 30) / Oculomotor control	L Computer generated; sealed opaque envelopes	H Carryover effects evident; authors suggest 1-week washout period may not have been sufficient	L Children, parents and provider not blinded; no deviations from intended intervention; ITT analysis used (participants with partial data included)	L 10% participants did not contribute any data and 40% partial data due to equipment calibration issues (balanced between groups)	H Sensitivity/ calibration of eye tracking equipment suboptimal for the participant group	L Prospective trial registration with reported outcomes/ measures pre- specified	High
Lynge 2021	Headache (n = 199) / Number of days per week with headache	L Computer generated; sealed opaque envelopes	N/A	L Children and parents blinded; provider not blinded; no deviations from protocol reported; mITT analysis used	L Complete weekly follow- up data available for 82% in both groups. Sensitivity analyses using multiple imputation for missing values show similar results to complete case analysis.	L Although participants were the outcome assessors, they were unlikely to have been aware of their intervention group assignment.	L Blinded interim analysis undertaken as per protocol; outcome reported in full	Low

Abbreviations: H = high risk of bias; L = low risk of bias; N/A = not applicable; ITT = intention to treat; mITT = modified intention to treat

#### Summary across studies

A summary of findings for all studies (original and updated review) is presented in Table 4.

#### Attention deficit hyperactivity disorder (ADHD)

We found very low certainty evidence about the effect of spinal manipulation on ADHD (as measured by reading time per sentence) (Cade 2021). Total reading time per sentence was shortened by 0.07 seconds in the group receiving manipulation, however the confidence interval is very wide, including both a decrease and increase in reading time (MD -0.07 seconds, 95% CI: from 1.08 fewer to 0.94 more seconds; 1 trial; 47 children¹). Adverse effects were not mentioned.

This study was primarily designed to test the feasibility of conducting an evaluation of oculomotor outcomes following SMT in children with ADHD. Several limitations were reported in relation to outcome measurement and study design. Three (10%) children were excluded from the analysis as they were unable to calibrate with the eye tracker for any outcome measure, and a further 12 children (40%) were unable to complete some parts of the assessment due to difficulties with equipment calibration. The study investigators also identified flaws with the crossover design of the trial, suggesting that the order each intervention was given may have contributed to the unexpected large group difference observed in reading time when comparing pre- and post-intervention scores. When comparing endpoint scores the difference in reading time observed between the groups was negligible. Further, in terms of the directness of the evidence, only 57% of the children in the study (17 out of 30) were aged under 12 years.

In the 2019 review, one study of children with ADHD (Accorsi 2014) found that manipulative therapy plus conventional care increased visual-spatial attention scores compared with conventional care alone, however the confidence interval was very wide, including both a decrease in attention and a potentially important increase. Since the outcomes measured in Accorsi 2014 and Cade 2021 were different we were unable to combine them in a meta-analysis.

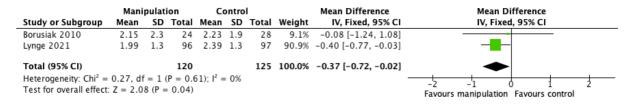
#### Headache

The study of 199 children and adolescents by Lynge 2021 (aged 7–14 years) was combined with an earlier study by Borusiak 2010 of 52 children and adolescents (aged 7–15 years). Both studies reported outcomes (number of days per week with headache and pain intensity) that could be combined in a meta-analysis.

We found low certainty evidence that spinal manipulation compared with sham SMT may reduce the mean number of days per week with headache among children aged 7 to 15 years (MD 0.37 days per week fewer, 95% CI: from 0.72 days to 0.02 days fewer per week; 2 trials; 245 children) (Figure 1). However, the confidence interval is compatible with both a small potentially important reduction and little or no difference.

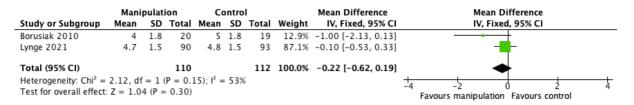
<sup>&</sup>lt;sup>1</sup> This was a crossover trial in which 30 children should have received both the intervention and active control (in random order). Due to equipment problems, not all children contributed data. Data were available for 23 children post intervention and 24 post control.

Figure 1. Number of days per week with headache (final values)



We found moderate certainty evidence that spinal manipulation compared with sham SMT probably results in little or no difference in headache pain intensity among children aged 7 to 15 years (MD 0.22 points lower, 95% CI: from 0.62 points lower to 0.19 points higher on a 10-point scale, lower score = less pain intensity; 2 trials; 222 children) (Figure 2).

Figure 2. Pain intensity (10-point scale; final values)



Lynge 2021 reported that 84% of children who received spinal manipulation and 75% who received sham manipulation had mild side effects of short duration after at least one consultation. There were no serious side effects.

#### Back and/or neck pain

Dissing 2019 was a secondary analysis of a trial of manipulative therapy in 238 Danish school children aged 9 to 15 years complaining of spinal pain. The main results paper (Dissing 2018) was included in the 2019 review and found low certainty evidence that the rate of recurrence of spinal pain may be higher among children who receive SMT compared to no SMT.

The secondary analysis explored five pre-specified effect modifiers and found that "children with long duration of spinal pain or co-occurring musculoskeletal pain prior to inclusion as well as low quality of life at baseline tended to benefit from manipulative therapy over non-manipulative therapy, whereas the opposite was seen for children reporting high intensity of pain. However, most results were statistically insignificant." Given the exploratory and hypothesis-generating nature of this secondary analysis, there is no change to our original assessment of this study.

#### Safety

The case report of a severe adverse effect involved an 8-year-old girl in the Philippines who received cervical manipulation from a massage therapist (qualifications unknown) for relief of asthma. The massage consisted of "repeated rotatory/twisting motions and digital pressure over the joints of the spine" after which the patient "developed intense neck pain ... with head locked and twisted towards the left." The girl was hospitalised with atlantoaxial rotatory subluxation but made a full recovery after being placed in a cervical orthosis for 6 weeks.

# Table 4. Summary of findings

## red rectangle = updated with new studies

# Spinal manipulation (SMT) compared to sham, no treatment or active comparator for any condition in children under 12 years of age

Patient or population: any condition in children under 12 years of age

Setting: healthcare setting (chiropractors in all studies)

Intervention: spinal manipulation (SMT)

Comparison: sham, no treatment or active comparator

	Anticipated abs	solute effects* (95% CI)				
Outcomes	Risk with sham, no treatment or active comparator	Risk with spinal manipulation (SMT)	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Crying time (infant colic) assessed with: crying diary completed by parents follow-up: range 8 to 14 days	The mean crying time was 2.7 hours per day <sup>a</sup>	MD <b>0.71 hours per day lower</b> (1.87 lower to 0.46 higher)	-	156 (3 RCTs)	⊕⊕⊖⊖ Low <sup>b,c,d</sup>	Spinal manipulation may reduce crying time by about 43 minutes per day (95% CI: from a reduction of 1 hour and 50 minutes to an increase of 28 minutes).1,2,3,e
Wet nights (nocturnal enuresis) assessed with: dry/wet diary completed by parents follow-up: mean 12 weeks	The mean wet nights was 11 per fortnight	MD 1.6 per fortnight fewer (3.21 fewer to 0.01 more)	-	46 (1 RCT)	⊕⊕⊖⊖ Low <sup>g,h,i</sup>	Compared to sham SMT, spinal manipulation may reduce bed wetting slightly, by one night per fortnight, (95% CI: from 3 nights fewer to 0 more) among children (5-13 years).4
Recurrence of spinal pain (back and/or neck pain) follow-up: mean 477 days	5 per 1,000i	6 per 1,000 (5 to 7)	Rate ratio 1.26 (0.98 to 1.61)	56486 (1 RCT) <sup>k</sup>	⊕⊕○○ Low <sup>l,m</sup>	Compared to no SMT, spinal manipulation may increase recurrences of spinal pain (back, neck or both) among children (9-15 years). If 10 children were followed for one year, 4 more recurrences may occur with spinal manipulation compared to no manipulation (95% CI: from 0 to 7 more recurrences, 238 participants).56
Days per week with headache Scale from: 0 to 7 follow-up: range 2 months to 3 months	The mean days per week with headache was 2.4 days per week	MD <b>0.37 days per</b> week fewer (0.72 fewer to 0.02 fewer)	-	245 (2 RCTs)	⊕⊕⊖⊖ Low <sup>n,o,p</sup>	Compared to sham SMT, spinal manipulation may reduce days per week of headache among children (7-15 years); however the confidence interval is compatible with both a small but potentially important reduction and little or no difference. <sup>7,8</sup>
Pain intensity (headache) assessed with: VAS or NRS Scale from: 0 to 10 follow-up: range 2 to 3 months	The mean pain intensity (headache) was 4.9 points	MD <b>0.22 points lower</b> (0.62 lower to 0.19 higher)	-	222 (2 RCTs)	⊕⊕⊕○ Moderate <sup>n,o</sup>	Compared to sham SMT, spinal manipulation probably results in little to no difference in headache pain intensity among children (7-15 years).7.8

# Spinal manipulation (SMT) compared to sham, no treatment or active comparator for any condition in children under 12 years of age

Patient or population: any condition in children under 12 years of age

**Setting:** healthcare setting (chiropractors in all studies)

Intervention: spinal manipulation (SMT)

Comparison: sham, no treatment or active comparator

	Anticipated abs	solute effects* (95% CI)				
Outcomes	Risk with sham, no treatment or active comparator	Risk with spinal manipulation (SMT)	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Peak expiratory flow (asthma) follow-up: mean 4 months	The mean peak expiratory flow was <b>104</b> % <sup>q</sup>	MD <b>0.7 % lower</b> (6.63 lower to 5.23 higher)	-	80 (1 RCT)	⊕⊖⊖⊖ Very low <sup>h,r,s</sup>	The evidence is very uncertain about the effect of spinal manipulation, compared to sham SMT, on pulmonary function among children (7-16 years).9,10
Days with otitis media symptoms assessed with: parent report (daily diary) Scale from: 0 to 28 follow-up: mean 4 weeks	The mean days with otitis media symptoms was 7	MD <b>2.5 more</b> (3.9 fewer to 8.9 more)	-	19 (1 RCT)	⊕⊕⊖⊖ Low <sup>t</sup>	Compared to sham SMT, spinal manipulation (SMT) may increase days with otitis media symptoms slightly among children (aged 6 months to 6 years); however, the confidence interval is wide and includes a decrease in symptom days and a large increase. 11
Muscle spasticity (cerebral palsy) follow-up: immediately after treatment	The mean muscle spasticity was 6.54 Newtons	MD <b>2.76 Newtons</b> lower (6.12 lower to 0.6 higher)	-	78 (1 RCT)	⊕⊖⊖⊖ Very low <sup>h,u,v</sup>	The evidence is very uncertain about the effect of spinal manipulation, compared to sham SMT, on muscle spasticity among children (8-18 years) with cerebral palsy. <sup>12</sup>
Reading time per sentence (ADHD) assessed with: computerised assessment tool follow-up: 7 days	The mean reading time per sentence was <b>3.44</b> seconds	MD <b>0.07 seconds</b> lower (1.08 lower to 0.94 higher)	-	47 (1 RCT)	⊕⊖⊖⊖ Very low <sup>h,w,x</sup>	The evidence is very uncertain about the effect of spinal manipulation (SMT) compared to sham SMT on reading time per sentence among children with ADHD. <sup>13</sup>
Attention scores (ADHD) assessed with: Visual-spatial attention test (Biancardi-Stroppa Modified Bell Cancellation Test) follow-up: mean 10 weeks	The mean attention scores (ADHD) was <b>110.5</b> points	MD <b>5.9 points higher</b> (7.97 lower to 19.77 higher)	-	28 (1 RCT)	⊕○○○ Very low <sup>h,y,z</sup>	The evidence is very uncertain about the effects of spinal manipulation plus conventional care, compared to conventional care alone, on attention scores for children (5-15 years) with a confirmed diagnosis of ADHD. <sup>14</sup>
Improvement of symptoms (torticollis) follow-up: mean 8 weeks	813 per 1,000	<b>796 per 1,000</b> (569 to 1,000)	RR 0.98 (0.70 to 1.39)	31 (1 RCT)	⊕⊖⊖⊖ Very low <sup>aa,ab,h</sup>	The evidence is very uncertain about the effect of spinal manipulation plus physiotherapy, compared to physiotherapy alone, on torticollis symptoms in infants (3-6 months). 15

# Spinal manipulation (SMT) compared to sham, no treatment or active comparator for any condition in children under 12 years of age

Patient or population: any condition in children under 12 years of age

Setting: healthcare setting (chiropractors in all studies)

Intervention: spinal manipulation (SMT)

Comparison: sham, no treatment or active comparator

	Anticipated absolute effects* (9	5% CI)			
Outcomes	Risk with sham, no treatment or active Risk with sp comparator manipulation	`	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Adverse events follow-up: range immediate to >1 years	Two trials, one on spinal pain and to other on asthma, reported that ther no adverse events. One trial on her reported minor adverse events: hot (SMT 6 children, placebo sham 9), dizziness (SMT 7, placebo sham 4) transitory increase in headache into and frequency (SMT 8, placebo sham 11 transitory increase in headache reporte side effects of short duration after a one consultation (SMT 84%, placel sham 75%) and no serious adverse effects. The trial on otitis media repriminimal self-limiting' adverse even back pain (SMT 1), irritability (SMT excessive crying (placebo 1). The remaining 10 trials did not report or adverse events (including the 3 trial infant colic).	e were adache skin  ensity am 6). ad mild tt least oo e orted ds: mid- 1),	951 (15 RCTs)	⊕○○○ Very low <sup>ac</sup>	The evidence about adverse events from randomised trials is very uncertain. Ten of 15 trials included for the effectiveness review did not mention (and may not have measured) adverse events. The remaining five trials reported no or minor adverse events.

<sup>\*</sup>The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). CI: confidence interval; MD: mean difference; RR: risk ratio

#### **GRADE Working Group grades of evidence**

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

#### Explanations

- a. Mean crying time with comparator was calculated from the mean crying time at final follow up in each of the three studies.
- b. Serious concerns (-1) about risk of selection bias (unclear randomisation in one study, unclear allocation concealment in two studies), and attrition bias (incomplete data for all studies, with greater attrition from control arms in two studies (31/99; 31%) compared to intervention arms (11/99; 10%)).
- c. Some inconsistency, but not downgraded because already downgraded for imprecision, which is influenced by inconsistent effects across studies.
- d. Serious concerns (-1) about imprecision. 95% confidence interval includes reduction in crying time of just under 2 hours per day and an increase of about half an hour per day. Number of participants is also less than optimal information size of approximately 400.
- e. Different comparators were used in each study (Browning 2008: occipito-sacral decompression (OSD); Olafsdottir 2001: no manipulation control wherein a nurse brought the baby to the chiropractor, then baby was undressed and held for 10 minutes (comparable to treatment); Wiberg 1999: dimethicone daily for 2 weeks [12-15 days]).
- f. Mean nights of bed wetting for comparator at final follow up in the single study.
- g. Serious concerns (-1) about risk of selection bias. No information about randomisation method or whether group allocation was concealed.
- h. Inconsistency could not be assessed (single study, not downgraded but results require replication in other studies).
- i. Serious concerns (-1) about imprecision. The 95% confidence interval includes a potentially important reduction in bed wetting (3 nights per fortnight) and a trivial increase. The number of participants is also less than the optimal information size of approximately 400.
- j. Events per 1000 patient days (not per 1000 people)
- k. Number of patient days (not number of participants)
- I. Serious concerns (-1) about indirectness. Participants' mean age was 12.6 years (eligibility 9 to 15 years) and results for children under 12 are not reported separately.

- m. Serious concerns (-1) about imprecision. 95% confidence interval includes no difference in recurrence and a small, possibly important increase. Number of participants is also less than optimal information size of approximately 400.
- n. No serious concerns about risk of bias. Most data come from Lynge (~90% weight in MA) which is at low risk of bias overall. Unexplained loss to follow in the intervention group (4/28 in the intervention group compared to 0/24 in the control group) in one trial, which contributes only 9% of weight in MA.
- o. Serious concerns (-1) about indirectness. Effects on younger children are very uncertain because both trials recruited older children (7-14 and 7-15; mean age ~10 and ~11 respectively). It is unclear what proportion of participants in the Lynge trial received spinal manipulation rather than pelvic and/or temporomandibular manipulation.
- p. Serious (-1) concerns about imprecision. The 95% confidence interval includes both a potentially important reduction in days per week with headache (0.72 fewer) and little or no difference (0.03 fewer).
- q. Peak expiratory flow (PEF) was measured in the morning prior to bronchodilator use. The mean control group value is the % PEF compared to baseline.
- r. Serious concerns (-1) about indirectness. Results are for children 7-16 years of age. Children 12 years and under comprise 66% (25/39) of the intervention group and 52% (22/42) of the comparator group.
- s. Very serious concerns (-2) about imprecision. The 95% confidence interval includes an increase in PEF and a decrease in PEF, both of which are small but potentially important. The number of participants is also less than the optimal information size of approximately 400.
- t. Very serious concerns (-2) about imprecision. 95% confidence interval includes a reduction in symptom days and a substantial increase. Number of participants is also less than optimal information size of approximately 400.
- u. Very serious concerns (-2) about indirectness. Outcomes were measured 15 minutes post-treatment, which is unlikely to be a clinically important time-frame for this population. The outcome measured is muscle tone, which may be less important to patients than functional outcomes.
- v. Serious concerns (-1) about imprecision. The 95% confidence interval includes a reduction in muscle spasticity and a trivial increase. The number of participants is also less than the optimal information size of approximately 400.
- w. Very serious concerns (-2) about risk of bias due to carry over effects of the intervention (when crossing over to receive control) and concerns about appropriateness of the measurement method.
- x. Very serious concerns (-2) about imprecision. 95% confidence interval is compatible with both an important reduction and an important increase in reading time
- y. Serious concerns (-1) about risk of selection bias (unclear allocation concealment) and performance bias (patients, parents and providers not blinded).
- z. Very serious concerns (-2) about imprecision. 95% confidence interval includes a reduction in attention score and a substantial increase. Number of participants is also less than optimal information size of approximately 400.
- aa. Serious concerns (-1) about risk of selection bias (unclear randomisation and allocation concealment), and risk of performance bias (manual therapist saw infants in both groups and was unblinded to treatment group).
- ab. Very serious (-2) concerns about imprecision. The 95% confidence interval includes both a potentially important improvement in torticollis symptoms and worsening of symptoms. The number of events is also much less than the optimal information size (300).
- ac. In most studies, the sample size is likely to be too small to detect less common adverse effects. The risk of bias across studies is very serious given that 10 trials did not mention (and potentially did not measure) adverse events.

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## References to new studies

#### Cade 2021

Cade A, Jones K, Holt K, Penkar AM, Haavik H. The effects of spinal manipulation on oculomotor control in children with attention deficit hyperactivity disorder: a pilot and feasibility study. *Brain Sci.* 2021;11(8). https://www.mdpi.com/2076-3425/11/8/1047

#### **Lynge 2021**

Lynge S, Hartvigsen J, Christensen HW, Vach W, Hestbaek L. Effectiveness of chiropractic manipulation versus sham manipulation on recurrent headaches in children aged 7-14 years: protocol for a randomized clinical trial. *Chiropr Man Therap*. 2019 Aug 23;27:40. doi: 10.1186/s12998-019-0262-y.

\*Lynge S, Dissing KB, Vach W, Christensen HW, Hestbaek L. Effectiveness of chiropractic manipulation versus sham manipulation for recurrent headaches in children aged 7-14 years: a randomised clinical trial. *Chiropr Man Therap*. 2021;29(1):1. https://chiromt.biomedcentral.com/articles/10.1186/s12998-020-00360-3

#### Pedro 2020

Pedro KM, Gaddi MJS, Sih IMY. Iatrogenic atlantoaxial rotatory subluxation after spinal manipulative therapy in a child. *Interdisciplinary Neurosurgery*. 2020;21:100721. <a href="https://www.sciencedirect.com/science/article/pii/S2214751920300104">https://www.sciencedirect.com/science/article/pii/S2214751920300104</a>

#### Dissing 2019 [secondary analysis of Dissing 2018]

Dissing KB, Vach W, Hartvigsen J, Wedderkopp N, Hestbæk L. Potential treatment effect modifiers for manipulative therapy for children complaining of spinal pain. Secondary analyses of a randomised controlled trial. *Chiropr Man Therap*. 2019;27:59.

https://chiromt.biomedcentral.com/articles/10.1186/s12998-019-0282-7

# Appendix 1. Primary studies of effectiveness

Study ID	Condition	Brief description and Author results/conclusions
Cade 2021 <sup>1</sup>	Attention deficit	17 children (8 to 11 yrs old) and 13 children (12 to 15 yrs old)
Crossover RCT	hyperactivity disorder	"Any spinal adjustments carried out were high-velocity, low-amplitude thrusts to the spine or pelvic joints, a standard spinal
Feasibility study		adjustment technique used by chiropractors."
		"The results indicate that the trial was feasible. Secondary outcomes showed that there was a significant decrease in reading time after the spinal manipulation intervention compared to the control intervention."
Lynge 2021 <sup>2,3</sup>	Headache	199 children (7 to 14 yrs old, mean 10.8 yrs)
RCT		"The chiropractic spinal manipulation treatment was directed at specific, individually identified dysfunctions of one or more joints in the spine, pelvis and/or temporomandibular joints. A <b>high-velocity</b> , <b>low-amplitude thrust</b> , <b>resulting in an audible cavitation</b> was given to improve the function of the joint."
		"Conclusions: Chiropractic spinal manipulation resulted in fewer headaches and higher global perceived effect, with only minor side effects."
Voloshyn 2022 <sup>4,5</sup>	Autism	269 children with autism spectrum disorder (mean age 6 yrs 9 mo).
Double-blind study Abstract only		"Patients divided in 4 groups: 1-control, 2-getting psychocorrectional approach, 3-psychopharmaceutical approach and 4-high-velocity low amplitude chiropractic intervention."
Classified as an "ongoing study"		"Results: All 3 groups (2,3,4) showed improvement in comparison to control. The most visible decrease in autistic traits happened in groups 2 (55.7 ATEC score before and 48.6 after), (p <0.01) and 4 (57.3 before and 49.7 after) (p <0.01)."
		"Conclusion: Using high-velocity low-amplitude chiropractic intervention may be more beneficial in comparison to using solely psycho-correctional techniques."
Dissing 2019 <sup>6</sup>	Back and/or neck pain	238 Danish school children aged 9-15 years complaining of spinal pain.
RCT Secondary analysis of existing study Dissing 2018		"We found that children with long duration of spinal pain or co- occurring musculoskeletal pain prior to inclusion as well as low quality of life at baseline tended to benefit from manipulative therapy over non-manipulative therapy, whereas the opposite was seen for children reporting high intensity of pain. However, most results were statistically insignificant."

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- 2. Lynge S, Hartvigsen J, Christensen HW, Vach W, Hestbaek L. Effectiveness of chiropractic manipulation versus sham manipulation on recurrent headaches in children aged 7-14 years, Protocol for a randomized clinical trial. Chiropr Man Therap. 2019 Aug 23;27:40. doi: 10.1186/s12998-019-0262-y.
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# Appendix 2. Included primary studies of safety

Study ID	Characteristics	Brief description
Pedro 2020 <sup>1</sup>	8-year-old girl Philippines Massage therapist	"One month prior to consult, the patient had aggressive manipulation of the neck."  "Plain cervical radiography showed an anterior
		displacement of the C1 lateral mass in relation to the odontoid process of C2."

- 1. Pedro KM, Gaddi MJS, Sih IMY. Iatrogenic atlantoaxial rotatory subluxation after spinal manipulative therapy in a child. Interdisciplinary Neurosurgery: Advanced Techniques and Case Management. 2020;21:100721.
  - https://www.sciencedirect.com/science/article/pii/S2214751920300104

# Appendix 3. Awaiting assessment (unclear if HVLA)

Study reference	Description
Kudryashova VG, Chetverikova NA. Study of the combined use of osteopathic correction and EEG-biofeedback training in children with attention deficit hyperactivity disorder. Russian Osteopathic Journal / Rossijskij Osteopatičeskij Žurnal 2022;56(1):60-68.  RCT English abstract; Russian full text.	70 children aged 6–9 years, suffering from attention deficit hyperactivity disorder.  Participants in both groups received EEG-biofeedback trainings. The participants of the main group additionally received a course of osteopathic correction.  Unclear if HVLA is involved.
Kamaletdinov VL, Kamaletdinova OV, Safin RF. Investigation of the osteopathic correction effectiveness in the treatment of pediatric patients with idiopathic <b>scoliosis</b> of the first degree. Russian Osteopathic Journal / Rossijskij Osteopatičeskij Žurnal 2022;56(1):23-34.  RCT English abstract; Russian full text.	50 patients aged 4 to 11 years with grade I idiopathic scoliosis.  The control group participants received standard orthopedic treatment, and the main group participants received <b>osteopathic correction</b> .  Unclear if HVLA is involved.
Parodi, V.; Carabetta, M.; Ottavi, G.; Briganti, S.; Prendy, E. Effect of osteopathic manipulative treatment on 44 newborns with <b>breastfeeding problems</b> . Journal of Maternal-Fetal and Neonatal Medicine 2021;34(SUPPL 1):22-23.  Case series with pre- and post-measurements Conference abstract only	44 newborns (0-3 months in term healthy babies). Every mother first received a lactation consultation (week 1) and then every child received 3 sessions of <b>osteopathic manipulative treatment</b> (one session every week for 3 weeks).  Unclear if HVLA is involved.

# Appendix 4. Excluded primary studies of effectiveness

Study ID	Condition	Exclusion reason	Description of intervention
Belsky 2022 Case series	Undergoing chemotherapy	Study design Intervention	'OMT consisted of myofascial release, muscle energy, balanced ligamentous tension, and visceral manipulation. Lymphatic pump and high velocity, low amplitude (HVLA) techniques were excluded.'
Bendixen 2021 Historical case- control	Hypothermia in neonates	Study design Intervention	'Specific OMT techniques were used at each provider's discretion and included a combination of myofascial release, balanced ligamentous tension, balanced membranous tension, and osteopathic cranial manipulative

			medicine.'
Blanco Díaz 2020 RCT	Constipation	Intervention	'Physical treatment consisted in the performance of manual physical therapy (MPT) protocol through direct and indirect articular, vascular, visceral, muscular, and myofascial techniques for the pelvic floor, abdomen (diaphragm, colon, and ileocecal valve, duodenojejunal flexure), skull, spine (D10–D12), and sacrum <b>exerting light pressure and vibration</b> , seeking a balance in fascial tensions.'
Castejón- Castejón 2019 RCT	Infantile colic	Intervention	'The <b>craniosacral therapy</b> intervention included the following techniques: balance of the pelvic, thoracic and clavicular diaphragms (transverse planes)'
Danielo Jouhier 2021 RCT	Breastfeeding	Intervention (HVLA?)	'The practitioner performed interventions on the part of the body considered appropriate, that is, muscles, bones or viscera.'  Note: intervention varied and was not well described. Potential that some infants may have received SMT, but SMT was not the primary purpose.
Holm 2021 RCT	Infantile colic	Intervention (HVLA?)	'The chiropractors were informed that manual therapy could include manipulation or mobilization of the spine and/or the extremities as they found indicated by the child's potential biomechanical dysfunctions, including movement restriction, tenderness or an obvious asymmetry in the muscles or joints. The treatment technique for restricted joint movements in this age group is, in general, very light short-term pressure with fingertips and gentle massage in case of hypertonic muscles.' Note: some infants may have received SMT in some cases but details are not provided.
Jones 2021 RCT	Asthma	Intervention	'Two techniques were used in each intervention patient: <b>rib raising and suboccipital release</b> .'
Lu 2019 RCT	Developmental delay	Intervention	'Stroking both sides of the spine with both hands from the top of the sacrum up to the base of the neck.'
Malak 2020 Case series	Autonomous nervous system	Study design Intervention	'During the CV4 procedure, the physiotherapist stood behind the infant, held the occipital bone and carefully approximated the lateral squama of the occipital bone towards the posterior occipital convexity and took the cranium into

			extension.'
Manzotti 2020 RCT	Prematurity (oxygen saturation and heart rate)	Intervention	'The second part of the procedure relies on the treatment, which is based on the palpatory findings of the initial assessment. Specifically, <b>indirect techniques</b> (e.g. cranial, functional, balanced ligamentous tension) were used.'
Marinelli 2019 Pre-post test	Prematurity	Study design Intervention	'The term "indirect technique" refers to a <b>gentle manipulative touch</b> (OMT) rather than a passive touch The purpose of the present study was to investigate whether OMT could improve or affect brain–splanchnic oximetry and function in LP infants, using near infrared spectroscopy (NIRS) monitoring before, during and after the OMT procedure.'
Mills 2021  Retrospective chart review	Newborn health	Study design Intervention	OMT 'consisted of articulation, direct and indirect myofascial release, balanced membranous tension, and balanced ligamentous tension.'
Pastor-Pons 2021 RCT [2 papers, same trial]	Plagiocephaly	Intervention	'The objective of the manual therapy protocol for the <b>upper cervical spine</b> was to mobilize the occiput, atlas and axis to restore ROM The practitioner applied a myofascial induction aiming to relax the cervical myofascial structures with a <b>gentle traction while gently assisting head movements</b> of flexion and extension, sidebending and rotation following the active and spontaneous movements of the baby. In all cases <b>end-range positioning into cervical extension and rotation were avoided</b> .'
Herzhaft-Le Roy 2016 RCT	Breastfeeding	Intervention	'In the treatment group, after assessing somatic dysfunctions and cranial strains based on tissue texture, tone, asymmetry, and quality of motion, active treatment was carried out, most commonly using techniques such as <b>balanced membranous tension</b> , <b>cranial sutures</b> , and <b>myofascial release</b> .'
Haiden 2015 RCT	Prematurity	Intervention	Visceral manipulative osteopathic treatment. 'The infant was always positioned in the supine position. The touch and focus was on the fascial tension of the abdomen'

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# Appendix 5. Excluded primary studies of safety

Ghanim MT, Bergmann S, Turner RD, Eskandari R, Mahajerin A. Recurrent Stroke in a Child With Atlantoaxial Instability Following Chiropractic Manipulation. J Pediatr Hematol Oncol. 2020;42(6):e518-e20. Case report. Purpose is to report on diagnostic imaging and does not attribute cause.

# Appendix 6. Systematic reviews of effectiveness

SR or Overview	Notes
Bagagiolo D, Rosa D, Borrelli F. Efficacy and safety of osteopathic manipulative treatment: an overview of systematic reviews. BMJ Open. 2022 Apr 12;12(4):e053468.	Included 2 SRs post 2018:  - Dal Farra 2020. Effectiveness of osteopathic interventions in chronic non-specific low back pain: A systematic review and meta-analysis. (10 RCTs all adults)  - Rehman 2020 Osteopathic Manual Treatment for Pain Severity, Functional Improvement, and Return to Work in Patients With Chronic Pain. (16 RCTs all adults)
Buffone F, Monacis D, Tarantino AG, Dal Farra F, Bergna A, Agosti M, Vismara L. Osteopathic Treatment for Gastrointestinal Disorders in Term and Preterm Infants: A Systematic Review and Meta-Analysis. Healthcare (Basel). 2022 Aug 12;10(8):1525.	Search to June 2021. Included 7 RCTs: Hayden 2006, Cerritelli 2013, Cerritelli 2015 (considered and excluded in 2019 review), *Haiden 2015, *Herzaft-LeRoy 2017, *Castejón-Castejón 2019, *Danielo Jouhier 2021); 1 retrospective cohort: Vismara 2019 (considered and excluded in 2019 SMT Review); 1 case-control: *Mills 2021 *See Excluded studies for these
Cascos-Vicente L, Juárez-Díaz E, Corral-Moreno V, Munuera-Jiménez FJ, et al. [Physiotherapeutic approach in the treatment of the infant colic. A systematic review.] Fisioterapia. 2022;44(3):184-91.	Abstract in English, article in Spanish. Author declined to provide a copy, citing 'journal owns the copyright' as the reason. Review included 13 RCTs "studies were classified according to the treatment applied (masotherapy, spinal manipulation, cranial manipulation, reflexology and acupuncture)."
Côté P, Hartvigsen J, Axén I, Leboeuf-Yde C, et al. The global summit on the efficacy and effectiveness of spinal manipulative therapy for the prevention and treatment of non-musculoskeletal disorders: a systematic review of the literature. Chiropr Man Therap. 2021 Feb 17;29(1):8.	Search to May 2019. Included 14 RCTs; 10 in adults 1 in childhood asthma (Balon 1998 – included in 2019 review) - 3 in infantile colic (Olafsdottir 2001, Wiberg 1999 – included in 2019 review; Miller 2012 – excluded from 2019 SMT Review)
DeMarsh S, Huntzinger A, Gehred A, Stanek JR, Kemper KJ, Belsky JA. Pediatric Osteopathic Manipulative Medicine: A Scoping Review. Pediatrics. 2021 Feb;147(2):e2020016162.	Search to September 2019. Included 1 study published in 2019: Kaiser G, Degenhardt BF, Michael Menke J, Snider KT. Characteristics and treatment of pediatric patients in an osteopathic manipulative medicine clinic. J Am Osteopath Assoc. 2020;120(3):153–163.

	"Descriptive data of paediatric patients receiving OMT from a neuromusculoskeletal medicine/OMM outpatient clinic."
Ellwood J, Draper-Rodi J, Carnes D. The effectiveness and safety of conservative interventions for positional plagiocephaly and congenital muscular torticollis: a synthesis of systematic reviews and guidance. Chiropr Man Therap. 2020 Jun 11;28(1):31.	Search to June 2019; no new SRs identified – includes Driehuis and Parnell Prevost (assessed in 2019 SMT Review).
Ellwood J, Draper-Rodi J, Carnes D. Comparison of common interventions for the treatment of infantile colic: a systematic review of reviews and guidelines. BMJ Open. 2020 Feb 25;10(2):e035405.	Search in 2019 (date not specified); no new reviews identified – includes Driehuis and Parnell Prevost (assessed in 2019 SMT Review).
Franke H, Franke JD, Fryer G. Effectiveness of osteopathic manipulative treatment for pediatric conditions: A systematic review. J Bodyw Mov Ther. 2022 Jul;31:113-133.	Search to July 2020; 47 RCTs, only 2 published post 2018: *Castejon-Castejon 2019 and *Manzotti 2020 *See Excluded studies for these
Perry R, Leach V, Penfold C, Davies P. An overview of systematic reviews of complementary and alternative therapies for infantile colic. Syst Rev. 2019 Nov 11;8(1):271.	Search to September 2018; no additional studies.
Maroye L, Klein P, Dethier C, Dugailly P. Osteopathic treatment of newborns and infants: efficiency and associated risks (a systematic review of literature in English and in French). Russian Osteopathic Journal. 2022;(2):133-148. (In Russian)	English abstract. Full-text in Russian.
Paknejad MS, Motaharifard MS, Barimani S, Kabiri P, Karimi M. Traditional, complementary and alternative medicine in children constipation: a systematic review. Daru. 2019 Dec;27(2):811-826.	Search to May 2019. One chiropractic study not considered previously: Alcantara J, Mayer DM. The successful chiropractic care of pediatric patients with chronic constipation: a case series and selective review of the literature. Clin Chiropr. 2008;11(3):138–47.
	Case series of 3 children <2 yrs. Full spine chiropractic care (high velocity low amplitude thrusts and the activator technique). AEs not declared.
Posadzki P, Kyaw BM, Dziedzic A, Ernst E. Osteopathic Manipulative Treatment for Pediatric Conditions: An Update of Systematic Review and Meta-Analysis. J Clin Med. 2022 Jul 30;11(15):4455.	Search to November 2021. Post-2018 studies: *Castejón-Castejón 2019, *Danielo Jouhier 2021, *Jones 2021, *Manzotti 2020, Rossi 2019
doi: 10.3390/jcm11154455. PMID: 35956072	Rossi, R.; Versace, A.; Lauria, B. The role of osteopathic complementary treatment in high frequency paediatric headache: A randomised controlled study. Neurol. Sci. 2019, 40, S231–S232 18 <b>teenagers</b> with paediatric headache.
	*See Excluded studies for these

# Appendix 7. Systematic reviews of safety

Corso M, Cancelliere C, Mior S, Taylor-Vaisey A, Côté P. The safety of spinal manipulative therapy in children under 10 years: a rapid review. Chiropr Man Therap. 2020 Feb 25;28(1):12.

Search to August 2019. Included studies of spinal manipulation (i.e. HVLA) and spinal mobilisation (low velocity). No additional studies identified.

Adverse events were described in five studies; with one study describing a severe adverse event (case report – Wilson 2012), one describing an indirect harm (case report – Shafir 1992), and three studies describing mild adverse events (one RCT – Sawyer 1999, one cohort study – Saedt 2007, one case series – Miller 2008).

Wilson 2012, Shafir 1992 and Miller 2008 were considered and excluded from the 2019 SMT Review. Sawyer 1999 was included in the 2019 SMT Review. Seadt 2007 considered adverse effects associated with 'mild mobilization techniques'.

# Appendix 8. Search strategies

We reviewed the PubMed search strategy used for the 2019 review to ensure that all 12 trials (with PubMed IDs) included in that review were retrieved by the revised search. The following changes were made to the original PubMed search:

- Applied the broader MeSH term Musculoskeletal Manipulations, which includes the MeSH terms Manipulation, Chiropractic and Manipulation, Spinal
- Truncated the textword infant\* (to retrieve infantile colic, etc.)
- Added the phrase "high velocity low amplitude" as textword
- Added "12 years" and "18 years" as textwords in the title/abstract

In place of searching Index to Chiropractic Literature (ICL) (for which we were unable to download records) we searched Ovid Emcare, a database specialising in nursing and allied health. All searches were run on 20 October 2022.

#### PubMed

(Musculoskeletal Manipulations[Mesh] OR "spinal manipulative" OR "spinal manipulation" OR "spine manipulation" OR "high velocity low amplitude" OR HVLA OR ((manipulat\*[TIAB] OR adjust\*[TIAB] OR manual\*[TIAB]) AND (spine[TIAB] OR spinal[TIAB] OR lumbar[TIAB]))) AND (Child[Mesh] OR Infant[Mesh] OR child[TIAB] OR children[TIAB] OR infant\*[TIAB] OR newborn\* OR neonate\*[TIAB] OR baby[TIAB] OR babies[TIAB] OR paediatric[TIAB] OR pediatric[TIAB] OR "12 years"[TIAB] OR "18 years"[TIAB]) AND 2019/06[EDAT]:3000/01[EDAT]

Records retrieved = 784

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#1	MeSH descriptor: [Musculoskeletal Manipulations] explode all trees	3374
#2	("high velocity low amplitude" OR HVLA):ti,ab,kw	261
#3	((manipulat* OR adjust* OR manual*) near spine):ti,ab,kw	692
#4	((manipulat* OR adjust* OR manual*) near spinal):ti,ab,kw	1321
#5	((manipulat* OR adjust* OR manual*) near lumbar):ti,ab,kw	339
#6	#1 OR #2 OR #3 OR #4 OR #5	4746
#7	MeSH descriptor: [Child] explode all trees	61999
#8	MeSH descriptor: [Infant] explode all trees	35185
#9	(child OR children OR infant* OR newborn* OR neonate* OR baby OR babies OR paediatric OR pediatric OR "12 years" OR "18 years"):ti,ab,kw	264026
10#	#7 OR #8 OR #9	264026
11#	#6 AND #10 with Publication Year from 2019 to 2022, in Trials	93

# Embase

# Embase Classic+Embase <1947 to 2022 October 17>

#	Search Statement	Results
1	exp Musculoskeletal Manipulation/	4650
2	(((spine or spinal or lumbar) adj5 (manipulat\$ or adjust\$ or manual\$)) or high velocity low amplitude or HVLA).tw.	5735
3	or/1-2	9448
4	Infant/	779538
5	Child/	2253178
6	(child or children or infant\$ or newborn\$ or neonate\$ or baby or babies or paediatric or pediatric or 12 years or 18 years).tw.	2983732
7	or/4-6	3889099
8	3 and 7	1071
9	limit 8 to yr="2019 -Current"	252

## AMED

# AMED (Allied and Complementary Medicine) <1985 to September 2022>

#	Search Statement	Results
1	exp Musculoskeletal Manipulations/	6472
2	(((spine or spinal or lumbar) adj5 (manipulat\$ or adjust\$ or manual\$)) or high velocity low amplitude or HVLA).tw.	1932
3	or/1-2	7241
4	exp Infant/	2282
5	exp Child/	19241
6	(child or children or infant\$ or newborn\$ or neonate\$ or baby or babies or paediatric or pediatric or 12 years or 18 years).tw.	28207
7	or/4-6	28207
8	3 and 7	371
9	limit 8 to yr="2019 -Current"	46

## Emcare

## Ovid Emcare <1995 to 2022 Week 40>

#	Search Statement	Results
1	exp Musculoskeletal Manipulation/	1602
2	(((spine or spinal or lumbar) adj5 (manipulat\$ or adjust\$ or manual\$)) or high velocity low amplitude or HVLA).tw.	3455
3	or/1-2	4554
4	Infant/	158489
5	Child/	599939
6	(child or children or infant\$ or newborn\$ or neonate\$ or baby or babies or paediatric or pediatric or 12 years or 18 years).tw.	948527
7	or/4-6	1082961
8	3 and 7	412
9	limit 8 to yr="2019 -Current"	117

#### CINAHL

#### CINAHL Plus via EBSCOhost

S1	(MH "Chiropractic+") OR (MH "Manipulation, Orthopedic") OR (MH "Manipulation, Osteopathic")	24,319
S2	TI ((spine or spinal or lumbar) N5 (manipulat* or adjust* or manual* ) OR AB ((spine or spinal or lumbar) N5 (manipulat* or adjust* or manual*))	3,608
<b>S</b> 3	TI ("high velocity lowamplitude" or HVLA) OR AB ("high velocity low amplitude" or HVLA)	334
S4	(MH "Child+")	752,490
<b>S</b> 5	TI ( child OR children ORinfant* OR newborn* ORneonate* OR baby ORbabies OR paediatric ORpediatric ) OR AB ( childOR children OR infant*OR newborn* ORneonate* OR baby ORbabies OR paediatric ORpediatric )	727,724
S6	S1 OR S2 OR S3	26,024
<b>S</b> 7	S4 OR S5	1,004,989
S8	S6 AND S7	1,471
<b>S</b> 9	S8 Limiters - PublicationYear: 2019-2022	185

#### SCOPUS

TITLE-ABS-KEY((((spine OR spinal OR lumbar) W/5 (manipulat\* OR adjust\* OR manual\*)) OR "high velocity low amplitude" OR hvla) AND (child OR children OR infant\*)) AND PUBYEAR > 2018