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**Spinal  
Manipulation  
for Infantile  
Colic**

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# Canadian Coordinating Office for Health Technology Assessment

## Spinal Manipulation for Infantile Colic

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## **Authorship**

Tammy Clifford, Peter Aker, Denis Leduc and Shaila Mensinkai contributed to the development of the systematic review protocol. Donald Husereau coordinated the systematic review team and was responsible for writing and revising the draft report through to the final version. Shaila Mensinkai was responsible for designing and executing the electronic literature search strategies; for writing the methods section and the appendix on literature searching; and for verifying and formatting bibliographic references. Donald Husereau and Tammy Clifford were responsible for selecting reports, judging their relevance, assessing their quality and extracting data from them. Tammy Clifford also provided expertise about the literature on colic and wrote most of the introduction. Peter Aker and Denis Leduc provided clinical expertise and contributed to the writing of the draft document, particularly the introduction and discussion; and its subsequent revisions.

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Laura McAuley led the development of the research protocol through to its final draft. The authors thank Chris Yelverton and his colleagues Sheree D. Koonin and Brent-Nolan Rubens, who graciously shared unpublished trial information with us. The authors are grateful to Dr. Pim Assendelft and Dr. Peter Lucassen of the Cochrane Collaboration, who provided feedback regarding search results. We are grateful for comments from Dr. Nils Grunnet-Nilsson of the University of Southern Denmark and Jennifer Bolton of the Anglo-European College of Chiropractic. We thank Mr. David Chapman-Smith for conducting a conference abstract hand search. In addition, we thank Scarlette Verjinschi for her assistance in providing telephone triage data and Dorothy Rhodes of IMS HEALTH, Canada, for providing drug utilization data.

## **Conflicts of Interest**

Donald Husereau: none

Tammy Clifford: none

Peter Aker: none

Denis Leduc: none

Shaila Mensinkai: none



# **REPORT IN BRIEF**

November 2003

## **Spinal Manipulation for Infantile Colic**

### **Technology Name**

Spinal manipulation for infant colic

### **Disease/Condition**

Colic in infants is characterized by excessive and inconsolable crying that appears between the second and sixth weeks of life. Despite being a common occurrence, colic remains a medical enigma. The causes are unknown and despite significant research, a “cure” has not been found. There is no “gold standard” for treating infant colic.

### **Technology Description**

Spinal manipulation involves quick, controlled techniques that are adapted for different ages and conditions. The force is applied by hand, suddenly rather than strongly, and moves the joint over a small range. In infants, the forces delivered are smaller than in adults and often only entail specific fingertip pressure. Spinal manipulation of infants is performed in an out-patient setting without the use of special equipment. Treatment usually involves more than one visit.

### **The Issue**

Up to 17% of families seek advice regarding their infant’s crying, contributing related costs to the health care system. Frequent episodes of infant colic can cause anxiety for parents and in some cases, excessive crying may trigger physical abuse such as that seen in “shaken baby syndrome.” A number of remedies for colic have been tried, including spinal manipulation. The use of spinal manipulation in children is controversial.

### **Assessment Objectives**

The objectives of this review are to determine:

- whether manipulating the spine, by itself, can reduce the signs and symptoms of infantile colic
- if spinal manipulation is safe.

### **Methods**

CCOHTA performed a systematic literature review to identify relevant clinical trials. Titles and abstracts were screened and eligibility criteria were applied. The criteria for inclusion focused on study design, participants, interventions, safety and measured outcomes. We evaluated the potential exaggeration of results from trial reports by applying Jadad’s scale and assessing if the randomization sequence was adequately concealed from investigators. An intention-to-treat analysis also helped in understanding the strength of findings.

### **Conclusions**

- There is no convincing evidence that spinal manipulation alone can affect the duration of infantile colic symptoms.
- The effect of spinal manipulation on sleep time, parental anxiety, quality of life and number of colic diagnoses could not be determined using available evidence.
- The potential harm from the spinal manipulation of infants with colic could not be determined using the evidence available from controlled trials.

This summary is based on a comprehensive health technology assessment available from CCOHTA’s web site ([www.ccohta.ca](http://www.ccohta.ca)): Husereau D, Clifford T, Aker P, Leduc D, Mensinkai S. **Spinal manipulation for infantile colic.**

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# EXECUTIVE SUMMARY

## The Issue

Infantile colic, which is characterized by excessive and inconsolable crying, is a common occurrence appearing between the second and sixth weeks of life. Up to one in six families may seek professional advice regarding a colicky infant. Parental anxiety created by the excessive crying may, rarely, trigger physical abuse such as that seen in “shaken baby syndrome.” A number of remedies for colic have been tried, including alternative treatments such as spinal manipulation. The use of spinal manipulation in children is controversial.

## Objectives

The objectives of this review are to determine whether manipulating the spine, by itself, can reduce the signs and symptoms of infantile colic and whether spinal manipulation is safe.

## Methods

Evidence was sought from controlled clinical trials of infants with colic by systematically reviewing the research literature. A trial was selected for review if it compared the effect of spinal manipulation on infants diagnosed with colic with that of other therapy. Any diagnosis of colic and any manipulation administered by a trained professional were acceptable. Reports of potentially relevant trials were identified after searching electronic databases, contacting experts and manually searching conference abstracts and reference lists of retrieved reports. A sensitive electronic search strategy was implemented on the DIALOG<sup>®</sup> system. Allied and Complementary Medicine<sup>™</sup> (AMED<sup>™</sup>), Manual, Alternative and Natural Therapy<sup>®</sup> (MANTIS<sup>™</sup>), MEDLINE<sup>®</sup>, EMBASE<sup>®</sup>, BIOSIS Previews<sup>®</sup>, PsycINFO<sup>®</sup>, PASCAL, SPORTDiscus, ExtraMed<sup>®</sup> and Dissertation Abstracts Online were searched. Searches were also run on the Index to Chiropractic Literature, CINAHL<sup>®</sup>, PEDro, the Cochrane Library, the Chalmers Research Group PEDCAM database, the Cochrane Complementary Medicine Field’s Register of Controlled Trials, the British Library Complementary Medicine Index and the University of York NHS Centre for Reviews and Dissemination. A request was submitted to the staff at the Research Council for Complementary Medicine, UK, to search<sup>©</sup> The Centralised Information Service for Complementary Medicine (CISCOM) database. The web sites of pediatric and chiropractic associations were searched. Searches were not restricted by language, date or publication status. Relevant trials were identified and the quality of each trial report was assessed independently by two reviewers. Information on trial design and the characteristics of the participants and interventions were also independently abstracted by two reviewers.

## Results

Of 66 potentially relevant reports identified, 62 were excluded because they did not meet the selection criteria. The four included reports described four randomized controlled trials. Two trials were published in peer-reviewed journals, one was a conference abstract and one was an unpublished manuscript. All trials involved spinal manipulation performed by chiropractors. The quality scores of all four reports, as measured by the Jadad scale (range zero to five, with five being the highest quality), were low (score=2 in both peer-reviewed reports and score=1 in the abstract and the unpublished manuscript).

The impact on the daily duration of colic symptoms was described in three reports. In a one-week trial that compared infants treated with spinal manipulation and standard counselling versus infants given sham manipulation and standard counselling from the same practitioner, a statistically significant difference in daily symptom duration between groups was not detected [3.1 hours (95% CI: 2.7; 3.5) versus 3.1 hours (95% CI: 2.6; 3.6) respectively]. Another one-week trial detected a statistically significant difference in the reduction of daily symptoms in infants with counselling and chiropractic versus counselling and medication (dimethicone) [2.7 hours (95% CI: 2.4; 3.0) versus 1.0 hours (95% CI: 0.6; 1.4) respectively].

In another trial, daily symptom duration after two weeks was reduced for a similar population of infants undergoing counselling, drug therapy and chiropractic care versus counselling and drug therapy [0.13 hours (95% CI: 0.03; 0.22) versus 2.7 hours (95% CI: 1.7; 3.7)].

None of the four controlled trial reports provided information about adverse effects during treatment. Nothing in the reports suggested that an adverse event had occurred, though it might not be labeled as such.

## **Conclusions**

- There is no convincing evidence that spinal manipulation alone can affect the duration of infantile colic symptoms.
- The effect of spinal manipulation on sleep time, parental anxiety, quality of life and the number of infants meeting diagnostic criteria for colic could not be determined using available evidence.
- The potential harm from the spinal manipulation of infants with colic could not be determined using evidence available from controlled trials.



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# 1 INTRODUCTION

## 1.1 Background

Infantile colic remains a medical enigma, despite its long history, its frequent occurrence and the abundant research that has been done to elucidate its etiology and to identify effective treatments. Though often trivialized because the condition tends to be self-limiting, colic may cause lasting changes to parent-child interactions and familial satisfaction, particularly in families whose resources are already strained.<sup>1-13</sup> In some cases, excessive crying from colic may be a trigger for physical abuse such as that seen in “shaken baby syndrome.”<sup>14-16</sup> Health care system costs related to colic can be substantial.<sup>17</sup> It is estimated that up to 21% of families have sought advice for their infant’s persistent crying.<sup>4,18-20</sup>

## 1.2 What is colic?

Colic is an ill defined condition that affects approximately 25% of infants.<sup>18,19,21-34</sup> It is characterized by excessive and inconsolable crying, hypertonicity and wakefulness, particularly in the evening. An infant with colic may draw up his or her knees, tense his or her body, sweat profusely and appear to be in pain. The onset of colic usually occurs between the second and sixth weeks of life. It tends to be a self-limiting condition, with most cases resolved by three months of age.

### 1.2.1 Rule of threes

The most widely cited definition of colic is the “rule of threes.”<sup>34-36</sup> The rule of threes defines a fussy infant as one who “otherwise healthy and well fed, had paroxysms of irritability, fussing or crying lasting for a total of three hours per day and occurring more than three days in any one week.” Infants are classified as “seriously fussy” if “their paroxysms continued to recur for more than three weeks or became so severe that the pediatrician felt that medication was indicated.”<sup>32</sup> Because most families and health care providers are unlikely to let an infant’s excessive crying continue for three weeks before forming a differential diagnosis of colic, the “three weeks” criterion is often omitted. Work by Barr suggests that this modified rule of threes (i.e., excluding the three-week criterion) is most frequently used in research on this topic.<sup>37</sup>

The daily duration of normal infant crying usually peaks at a median of 2.75 hours during the sixth week of life, then decreases around the fourth month.<sup>36,38-41</sup> This pattern is commonly called the “normal crying curve.” Whether the crying of infants with colic is a distinct clinical entity or simply the upper limit of the normal crying curve is uncertain. Empirical evidence, however, supports the rule of threes’ distinction between “fussy” and “contented” infants.<sup>36</sup> This, with evidence that the daily duration of crying is the chief complaint of parents,<sup>12,20,42</sup> suggests that it is most appropriate to focus on the quantitative aspects of infants’ crying or fussing patterns when studying colic.

## 1.3 Current Clinical Practice

Although a large amount of literature describing the effectiveness of interventions for colic has been published, a “cure” has not been found. Interventions tend to be undertaken on a trial-and-error basis, with parents moving from one treatment modality to another until the colic disappears of its own accord. Three systematic reviews have outlined limitations in the quality and quantity of evidence on the pharmaceutical, dietary, behavioural or naturopathic remedies for colic.<sup>43-45</sup>

### 1.3.1 Physicians

Physicians provide the diagnosis of and management strategies for infant colic. Physicians can perform a physical examination to exclude other causes for excessive crying and reassure parents of their child’s normal growth and development. Once a diagnosis of colic is confirmed, clinicians should acknowledge the parents’ frustration. The provision of information about age-appropriate crying behaviours may enable families to better cope during this difficult time. Because of the association of excessive infant crying and physical abuse, the physician may also seek signs of parental distress, particularly in families with inadequate resources or coping abilities.<sup>16</sup>

It is difficult to estimate the extent of physician-based care for colic in Canada. Few provincial jurisdictions use a service code for its diagnosis and management. We are unaware of any published Canadian surveys.<sup>14,15</sup>

### 1.3.2 Pharmacists

Pharmacists may receive requests from parents or caregivers who are exasperated by an infant’s inconsolability. No evidence, however, supports the effectiveness of any pharmacological agent for the treatment of colic. Dicyclomine, an antispasmodic medication that was widely used in the 1950s, 1960s and 1970s, is now contraindicated for infants because of reported adverse effects that include respiratory collapse, apnea, seizures and coma.<sup>46</sup> Another drug, simethicone, has been investigated as a remedy for colic, because it alters the surface tension of gas bubbles in the intestinal tract, thereby facilitating their dispersion.<sup>47</sup> The evidence suggests, however, that simethicone is no more effective than placebo in reducing colic, with the natural history of colic being an improvement over time.<sup>48,49</sup> Despite this, Canadians spent roughly \$1,000,000 on one brand of this drug alone in 2002. In the same year, over 1,600 prescriptions were dispensed for the same product (Dorothy Rhodes, IMS HEALTH, Pointe-Claire (QC): personal communication, 2003 May 26).

### 1.3.3 Chiropractors

Chiropractic care is one of the most commonly used forms of alternative medicine in North America.<sup>50</sup> In Canada, chiropractors are primary contact health care practitioners, i.e. parents do not need a referral from a physician to seek a diagnosis and treatment of health problems from a chiropractor. While most patients seek help from a chiropractor for musculoskeletal problems (e.g. back pain, neck pain) or headache, about 5% use chiropractic services to manage non-musculoskeletal health problems.<sup>51</sup>

In 1999, survey (n=643) and diary (n=490) records of a random sample of Canadian chiropractors were used to determine their involvement in the treatment of children.<sup>52</sup> In the survey, about 46% of chiropractors stated that they treated infants with colic, but the diaries indicated that about 15% actually treated a median of one infant per month for colic. Even though these data are limited, we can use these figures to estimate that up to 7,000 colicky infants are treated each year by chiropractors in Canada.

In another survey, Alberta chiropractors were presented with vignettes of pediatric disorders. For a vignette describing an infant with colic, 52% responded that they would initiate treatment, 35% would provide care in collaboration with a conventional health practitioner and 10% would not treat or would refer the child elsewhere.<sup>53</sup> In almost all cases, chiropractors indicated that spinal manipulative therapy would be the primary form of treatment used if they initiated care.<sup>53</sup>

### **1.3.4 Nurses and counselling**

An infant's excessive crying can adversely affect his or her parents.<sup>1-13</sup> Moreover, unless there is successful resolution to the colic problem, frustrated parents may respond to their infants in a disorganized manner, potentially exacerbating their infants' crying. Counselling has involved reassurance to parents that their child is not sick; and education about the patterns of crying and about being more "effectively" responsive by reducing the amount of picking up and feeding, while increasing the amount of independent soothing (e.g. pacifier, hot water bottle, heating pad).<sup>54-58</sup> Behaviour modification may create consistency and promptness of maternal response, which have been associated with reduced frequency and duration of crying. Trials of these interventions have led to inconsistent results.<sup>59,60</sup>

Nurses in both community health and larger triage centres play an important role in providing counselling to parents of a newborn. However, one provincial telephone triage centre reported receiving only a small proportion (one to two per 20,000 calls) for infant colic for the period of January 2003 to and including April 2003 (Scarlette Verjinschi, Ministry of Health Planning, Victoria: personal communication, 2003 May 28).

### **1.3.5 Other complementary health care or parent-based treatments**

Pharmacists, physicians, nurses, chiropractors and other primary health practitioners may recommend a variety of interventions for colic. Parents may also initiate treatments after talking to peers or after seeking information. Available therapies include but are not limited to herbal teas,<sup>61</sup> sucrose,<sup>62</sup> gripe water, dietary modifications including fibre-enriched formulas,<sup>63</sup> reduced lactose formulas,<sup>64</sup> soy,<sup>65,66</sup> hydrolyzed formulas,<sup>67-71</sup> specific sources of infant nutrition (e.g., breast milk, formula),<sup>57</sup> increased carrying,<sup>60</sup> music,<sup>72,73</sup> vibration or massage<sup>74</sup> and pacifiers (or soothers).<sup>75</sup>

## 1.4 Economic Impact in Canada

Utilization data are unavailable for an estimate of the economic burden of infantile colic. Components of the direct costs associated with two weeks of treatment are shown in Table 1.

**Table 1:** Direct costs associated with two weeks of infantile colic therapy

Cost Item	Cost (\$)	Units Consumed	Total Costs, Range (\$)
	Low to high estimate	Low to high estimate	
No treatment	0 to 0	N/A	0
Pharmacist- or parent-based care <sup>1</sup>			
Simethicone	6.99 to 10.99	1 to 3	6.99 to 32.97
Homeopathic	5.99 to 15.99	1 to 5	5.99 to 79.95
Gripe water	1.99 to 3.49	1 to 4	1.99 to 13.96
	Total		1.99 to 126.88
Physician visit <sup>2</sup>			
Family physician: first consultation and treatment	27.30 to 54.75	1	27.30 to 54.75
Specialist: first consultation and treatment	27.30 to 112.35	1	27.30 to 112.35
Subsequent treatments	27.30 to 34.65	1 to 4	27.30 to 138.60
	Total		27.30 to 250.95
Spinal manipulation (chiropractic) <sup>3</sup>			
Initial consultation, examination and treatment	11.75 to 61.75	1	11.75 to 61.75
Subsequent treatment	9.65 to 29.65	2 to 5	19.30 to 148.25
	Total		11.75 to 210.00

<sup>1</sup>Price based on retail price before applied provincial or federal sales tax. <sup>2</sup>Physician fee schedule based on Ontario Health Insurance Plan fee schedule and authors' consensus. <sup>3</sup>Based on Ontario fee schedule and reasonably discounted fees according to authors' consensus.

A report from the UK estimates that persistent infant crying costs society the equivalent of C\$216 (95% CI: \$168; \$264) on average per infant (regardless of the presence of colic).<sup>17</sup> There are no published Canadian data on the financial burden of infant crying or colic on society or on the health care system.

## 1.5 Technology Overview

The use of spinal manipulation and other alternative medicines in children remains controversial.<sup>76,77</sup> Systematic reviews try to answer clinical questions while minimizing potential reviewer bias.<sup>78</sup> We are unaware of a systematic literature review that examines the outcome of spinal manipulation in infants for colic, so we opted to conduct such a review using the best available methods.<sup>79</sup> We sought to determine the effect of spinal manipulation alone (efficacy) rather than the effect of an approach where spinal manipulation is integrated with other forms of treatment.<sup>80</sup>

### 1.5.1 Description of the technology

Spinal manipulation includes joint adjustments, mobilization, manual traction, trigger point therapy and other soft tissue techniques.<sup>81</sup> In spinal manipulation, the quick, controlled techniques used are adapted for different spinal regions, ages and conditions. The force, which is applied suddenly rather than strongly, moves the joint over a small range. The degree of movement is similar to that experienced when you “crack” a finger joint. In infants, the forces delivered are smaller than those in adults and often only entail specific fingertip pressure. Accurate control of the direction, speed and magnitude of the thrust is a learned skill.<sup>82</sup>

The indications for spinal manipulation are the presence of aberrant motion (dysfunction) in the articulations of the spine, with or without local or distant musculoskeletal signs such as tenderness or spasm. The presence of signs or symptoms of another disease, spinal deformity or neurologic abnormality may preclude the use of manual therapies.

Our purpose in this review is not to focus on the poorly understood mechanism(s) by which manipulation might affect visceral conditions such as colic. Clinical observations in the early 1900s, with reports of improvement from more recent uncontrolled, observational studies,<sup>83-85</sup> stimulated further research in this area. Although many theories exist, an accepted explanation involves viscerosomatic and somatovisceral spinal reflexes, wherein a structural or functional disturbance in the spine leads to a disturbance in nerve transmission. This in turn leads to symptoms of internal organ dysfunction or disease. Correction of the spinal irritation by manipulation is thought to remove the somatovisceral reflex and hence improve internal organ function.<sup>86,87</sup> Any theory requires further clinical and experimental research to establish its validity.

Spinal manipulation is practised by chiropractors, family physicians, osteopaths, orthopedic specialists and physical therapists. Practitioners may have varying amounts of training. We sought to assess the effect of manipulation, regardless of the training of the individual who performed it or the technique employed. We did not focus on chiropractic techniques, although these might be the techniques that are used most often.

Spinal manipulation of infants is performed in an out-patient setting without the use of special equipment. Treatment usually involves more than one visit. The dosage and duration of manipulative procedures have not been empirically determined or standardized.

## 2 OBJECTIVES

The objective in this project is to answer the following questions:

- Does spinal manipulation alone reduce the signs and symptoms of infantile colic?
- Is spinal manipulation of infants for colic safe?

To find the answer, evidence was sought from controlled clinical trials of infants with colic through a systematic review of research literature.

## 3 CLINICAL EFFECTIVENESS REVIEW

### 3.1 Methods

#### 3.1.1 Literature search strategy

Searches were conducted on the following DIALOG<sup>®</sup> system databases: Allied and Complementary Medicine<sup>™</sup> (AMED<sup>™</sup>), Manual, Alternative and Natural Therapy<sup>®</sup> (MANTIS<sup>™</sup>), MEDLINE<sup>®</sup>, EMBASE<sup>®</sup>, BIOSIS Previews<sup>®</sup>, PsycINFO<sup>®</sup>, PASCAL, SPORTDiscus, ExtraMed<sup>®</sup> and Dissertation Abstracts. This resulted in 181 unique records. Please see Appendix 1 for the detailed search strategy.

The search was not restricted by language, year or publication status. Clinical and infant filters were initially used, but they were removed from the original strategy due to the small number of reports identified. DIALOG<sup>®</sup> alerts were established until April 2003 on the databases to capture newer citations. PubMed was also periodically searched to capture additional references. A final search was performed and reviewed before the report was peer-reviewed.

Searches were run on the Index to Chiropractic Literature, CINAHL<sup>®</sup>, PEDro and the Cochrane Library. Many records from these searches were duplicates of those found in the DIALOG<sup>®</sup> search.

A request was submitted to the Research Council for Complementary Medicine, UK to search ©The Centralised Information Service for Complementary Medicine (CISCOM) database. Keywords and terms were submitted with the search request. The project team also searched the PedCAM database (a Reference Manager database of randomized controlled trial reports in pediatric complementary and alternative medicine) maintained by the Chalmers Research Group in Ottawa. Search results from these databases were duplicates of those identified by the DIALOG<sup>®</sup> search.

Grey literature (unpublished studies with limited distribution) was sought by searching the web sites of health technology assessment and related agencies. We searched the web sites of pediatric and chiropractic associations, including the American Chiropractic Association, Foundation for Chiropractic Education and Research, World Federation of Chiropractic,

American Academy of Pediatrics and Canadian Paediatric Society. These searches were supplemented by specialty database searching, such as those of the Cochrane Complementary Medicine Field Registry of Randomized Controlled Trials, the British Library Complementary Medicine Index and the University of York NHS Centre for Reviews and Dissemination.

One reviewer (DH) manually searched available conference proceedings at the CC Clemmer Health Sciences Library of the Canadian Memorial Chiropractic College in Toronto, Ontario. These included Proceedings of the International Federation of Orthopedic Manipulative Therapy (1977), Proceedings of the Scientific Symposium on Spinal Biomechanics (1990, 1991), Proceedings of the International Conference on Spinal Manipulation (1992, 1993, 1994, 1996, 1998), Proceedings of the Foundation for Chiropractic Education and Research (2000) and Proceedings of the Fifth Biennial World Federation of Chiropractic Conference (1999).

One reviewer (TC) searched the references of all articles selected for inclusion. She also manually searched the following conference proceedings: Canadian Paediatric Society Annual General Meeting in “Paediatrics and Child Health” for 1997 to 2002 inclusive; “Pediatric Research” (contains the conference proceedings of the joint meetings of the American Pediatric Society, Ambulatory Pediatric Association, European Society for Paediatric Research and Society for Pediatric Research, 1987 to 2002 inclusive); the Society for Pediatric and Perinatal Epidemiologic Research in “Paediatric and Perinatal Epidemiology” (searched 1989 to 1992 and 2001 to 2002) and SDBP (Society for Developmental and Behavioral Pediatrics, searched 1984 to 2002 inclusive).

Individuals and organizations identified as having specialized knowledge of spinal manipulation or its associated literature were sent e-mails or contacted by telephone. These included Brian Berman of the Cochrane Complementary Medicine Field, Niels Grunnet-Nilsson of the University of Southern Denmark, Jennifer Bolton of the Anglo-European College of Chiropractic, Howard Vernon of the Canadian Memorial Chiropractic College, David Chapman-Smith of the World Federation of Chiropractic, Gert Bronfort of the Northwestern University of Health Sciences, Allan Gotlib of the Journal of the Canadian Chiropractic Association and Jeff Balon of the Holistic Clinic, Ottawa.

### **3.1.2 Selection process**

Citations identified through the electronic database and manual searches were imported into a Reference Manager<sup>®</sup> database, with duplicates removed manually. These citations were then exported to a web-based system for data screening and duplicates manually removed.

Two reviewers (DH and TC) systematically and independently screened the titles and abstracts of all citations captured in the initial search. The web-based system displayed the title and abstract only and then asked four questions:

1. Does the study deal with infantile colic (yes, no, unclear)?
2. Does the study involve spinal manipulation (yes, no, unclear)?
3. Is there a comparator group (yes, no, unclear)?
4. Are there original data (e.g. a review or comment may not present original data) (yes, no, unclear)?



If both reviewers concluded that a citation did not meet one of the eligibility criteria for review, the citation was excluded. In case of doubt on the part of either reviewer, the original report was retrieved for further assessment.

### **3.1.3 Selection criteria**

After the initial screening procedure, the eligibility criteria were applied systematically to all retrieved reports. A trial was selected for inclusion if it was independently judged by both reviewers to meet the criteria. Trials written in languages other than English were translated into English before assessment.

#### **a) Study design**

All comparative trials had to include infants with colic, with at least one treatment arm being spinal manipulation and one treatment arm being any other comparator, regardless of language of publication, date or publication status.

#### **b) Participants**

Participants had to include infants with diagnosed colic. Any definition of colic used in the publication was accepted. Details about the diagnoses were recorded to assess the comparability of diagnoses between studies.

#### **c) Interventions**

Interventions had to involve any use of spinal manipulation by an individual identified as a trained professional versus any comparison group.

Types of Outcomes: Trials that captured one of the following outcomes were identified for inclusion:

#### Primary Outcomes

1. Signs and symptoms of infantile colic: The most commonly used research definition of infantile colic involves symptoms of crying and fussing. Thus, the signs and symptoms of interest were:
  - crying time per week
  - fussing per week
  - crying and fussing time per week (since these may be measured or reported together).
2. Safety: The number or type of adverse events reported.

#### Secondary Outcomes

1. Sleep time
2. Parental anxiety and quality of life
3. Proportion of participants no longer fulfilling criteria for diagnosis of colic.

### **3.1.4 Data abstraction**

For each included trial, information on trial design, participant characteristics and interventions was abstracted by two reviewers (DH and TC) independently onto an electronic spreadsheet that included headings from the list shown in Appendix 2. Disagreements were resolved by

consensus. A third party was available but unnecessary to resolve persisting differences. Missing or unclear information was sought by e-mail from the investigators in the clinical trials. The authors' names and titles of the reports were not masked when data abstraction was performed.

### **3.1.5 Quality assessment of the evidence**

The quality of each trial report was assessed independently by two reviewers (DH and TC). A three-item Jadad instrument (Appendix 3) was used to assess the reporting of randomization, blinding and withdrawals. The Jadad scale was used to rate the quality of trial reports on a scoring system of zero to five, five being the highest quality. The presence or absence of an intention-to-treat (ITT) analysis – defined as one in which all participants in a trial were analyzed according to the intervention to which they were allocated, whether they received it or not – was noted. Allocation concealment as an indicator of methodologic quality was assessed as adequate, inadequate or unclear. Every attempt was made to assess quality by using supplemental information from other reports or by contacting trial investigators by e-mail. As the reviewers were familiar with quality scoring and assessment methods, a calibration exercise was not conducted beforehand. The potential caveats, however, were discussed.

### **3.1.6 Data analysis**

Meta-analysis was impossible because of clinical heterogeneity in patient groups, comparators and reported outcomes, although meta-analysis using a random effects model was planned. Similarly, a chi-square test to detect statistical heterogeneity for meta-analyzed outcomes and a funnel plot analysis to detect the possibility of publication bias were planned, but these could not be performed. No subgroup or sensitivity analysis was planned. In keeping with statistical and clinical principles, an analysis based on ITT information from each trial, where possible, was planned.

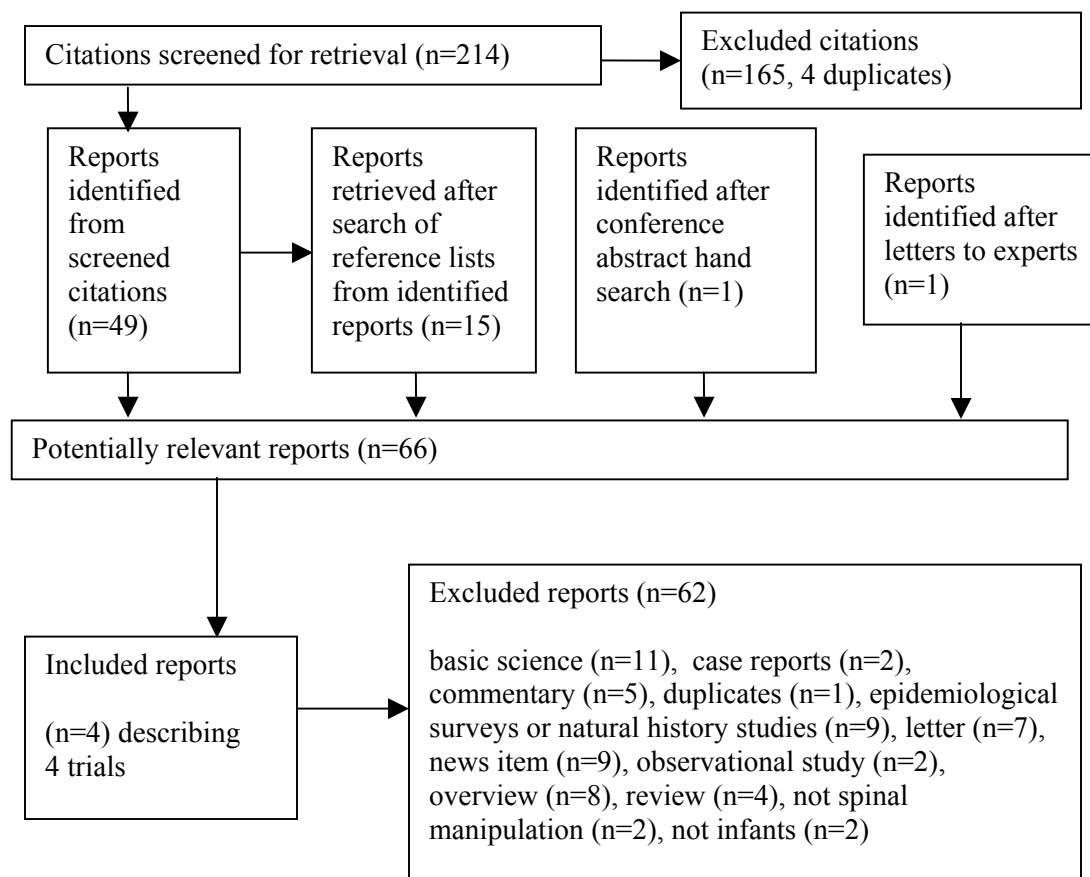
Because meta-analysis was impossible, a planned comprehensive qualitative synthesis involving a textual description and a tabular presentation of study-specific characteristics was prepared. This synthesis highlighted the bases on which the individual trials varied. It painted a picture of clinical heterogeneity or comparability of the included studies and provided insight into the decision to not pool trial results.

## **3.2 Results**

### **3.2.1 Quantity and quality of research available**

A search of electronic databases identified 214 citations, of which, 165 citations were excluded. After manually searching the reference lists of the 49 retrieved reports, 15 additional citations were identified. A report of one additional trial was identified after a hand search of conference abstracts. One new trial was identified through contact with experts in the field. The inclusion and exclusion of trial reports are depicted in Figure 1. A large randomized controlled trial that fulfilled our selection criteria is ongoing (excluded from the flowchart).<sup>88</sup> It involves 300 infants diagnosed with colic who are less than six weeks old and who will be manipulated by a chiropractor. Excluded citations with reasons for exclusion are listed in Appendix 4.

**Figure 1:** Flow diagram of inclusion and exclusion of trial reports



Two trials<sup>89,90</sup> (from Norway and Denmark) were published in peer-reviewed journals and were identified from the initial electronic search. Two other trials<sup>91,92</sup> were conducted in South Africa; one was published in abstract form and identified from manual searching and the other was identified and the manuscript was obtained for supplemental information after correspondence with one of the authors (Chris Yelverton, Technikon Witwatersrand, Doornfontein, South Africa: personal communication, 2003 Jan 23). All were published in English. Information about the published reports and abstract was also available from other reports.<sup>93</sup> There was 100% agreement between reviewers regarding study relevance. Characteristics of the diagnostic and treatment schedules in each trial are shown in Table 2. Characteristics of the four trials are shown in Table 3.

Quality scores were low in all four trials. All trials were described as randomized, but none provided a detailed or appropriate method of randomization. None were described as double-blinded. Three trial reports adequately described withdrawals and drop-outs. Reviewer agreement was 100% regarding the quality of the trials (Table 4).

Concealment of the randomized treatment allocation sequence was judged by both reviewers to be inadequate in the studies by Wiberg *et al.* and Koonin *et al.* and unclear in the remaining two trials. Supplementary information<sup>94</sup> indicated that randomization was adequately concealed in the trial by Olafsdottir *et al.*

**Table 2:** Characteristics of diagnosis and intervention in included trials

	<b>Main Diagnostic Criteria for Colic</b>	<b>Who Performed Diagnosis?</b>	<b>Spinal Manipulation Technique</b>	<b>Who Performed Spinal Manipulation?</b>	<b>Duration and Frequency of Spinal Manipulation</b>
Koonin <i>et al.</i> <sup>92</sup> (Sheree Debbie Koonin, Technikon Witwatersrand, Doornfontein, South Africa: personal communication, 2003 Oct 02)	≥3 hours of crying per day, ≥3 days per week, over last three weeks	Pediatrician	“All infants received [high velocity, low amplitude] chiropractic spinal manipulation”	Chiropractor	Maximum six treatments (every two to three days) over two weeks
Mercer <i>et al.</i> , <sup>91</sup> 1999	“diagnosed as suffering from infantile colic by pediatrician”	Pediatrician	NR	Chiropractor	Maximum six treatments over two weeks
Olafsdottir <i>et al.</i> , <sup>89</sup> 2001	≥3 hours per day, ≥3 days per week, over last three weeks	NR	“Dysfunctional articulations were manipulated and mobilized using light fingertip pressure”	Chiropractor	Three treatments at intervals of two to five days for eight days
Wiberg <i>et al.</i> , <sup>90</sup> 1999	≥1 violent crying spells daily, ≥3 hours per day for five of seven previous days	Health visitor nurse (structured interview)	“...[Restricted] articulations manipulated or mobilised with specific light pressure with the fingertips”	Chiropractor	Three to five treatment sessions for up to two weeks

NR=not reported

Of the two published trials, one was funded by the Norwegian Research Council<sup>89</sup> and the other was funded by the Danish Health Insurance Fund and the research committee of the Danish Chiropractors’ Association.<sup>90</sup> The authors of the unpublished manuscript indicated that their study was funded by their chiropractic clinic.<sup>92</sup>

The decision to conduct a strict ITT analysis was not described in any report. It was unclear from the text of the abstract if an ITT analysis was planned. The authors of one published report re-analyzed data *post hoc* according to ITT and detected no statistical difference between groups.<sup>89</sup> In the other published report,<sup>90</sup> five drop-outs were reported in the dimethicone treatment arm (20%). The authors stated in their discussion that the performance of dimethicone would appear even less favourable when compared with chiropractic if the data were re-analyzed according to the ITT principle. Results from a re-analysis, however, were not reported.

**Table 3:** Characteristics of four controlled clinical trials identified for inclusion in this review

Study	Setting, Design	Number of Participants, ITT (analyzed)			Duration of Colic Symptoms at Baseline, Weeks (SD)	Age of Infants at Baseline, Weeks (SD)	Intervention	Outcomes	Quality assessment	
		Total	Treatment	Control					Jadad Score	Allocation Concealment
Koonin <i>et al.</i> , 2001 <sup>92</sup> (Sheree Debbie Koonin, personal communication: 2003 Oct 02)	South Africa, Randomized, unblinded, controlled parallel group study	31	15	16 (15)	Treatment 1.87 (NR) Control 2.03 (NR)	Treatment 5.7 (NR) Control 5.9 (NR)	Treatment: counselling + prescribed medicine + chiropractic referral  Control: counselling + prescribed medicine	Duration of crying per day, frequency of crying per day, total crying per day, improvement on ordinal scale as reported by parental questionnaires pre-treatment, post-treatment and at follow-up	1	Inadequate
Mercer <i>et al.</i> , <sup>91</sup> 1999	South Africa, Randomized, unblinded, placebo controlled, parallel group	30	15 (NR)	15 (NR)	NR	Between zero and eight weeks	Treatment: chiropractic spinal manipulation  Control: non-functional de-tuned ultrasound machine	Proportion of infants with complete resolution of symptoms reported in one treatment arm	1	Unclear
Olafsdottir <i>et al</i> , <sup>89</sup> 2001	Norway, Randomized double-blinded, placebo controlled, parallel group	100	50 (46)	50 (40)	Treatment 3.6 (1.5) Control 4.3 (1.9)	Between three and nine weeks	Treatment: counselling or clinical examination + chiropractic manipulation every two to five days for eight days  Control: counselling or clinical examination + sham manipulation <sup>a</sup> every two to five days for eight days	Parent's report to a pediatrician of response to treatment at each visit using categorical responses on an ordinal scale  Parent's 24-hour diary of infant's crying	2	Unclear

Wiberg <i>et al.</i> , <sup>90</sup> 1999	Denmark,  Randomized, unblinded, controlled, parallel group trial	50	25 (25)	25 (20)	Treatment 3.7 (3.6) Control 3.7 (2.5)	Treatment 5.9 (3.1) Control 4.9 (2.5)	Treatment: counselling from a health visitor nurse + referral to a chiropractor for two weeks  Control: counselling from a health visitor nurse + dimethicone daily for two weeks as indicated	Percent change in each child mean hours of infantile colic behaviour per day as registered in 24-hour diary  Parent's report to health visitor nurse after each week of treatment	2	Inadequate
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SD=standard deviation. NR=not reported. <sup>a</sup> Sham manipulation in this instance consisted of being held by a nurse for 10 minutes (the approximate time of treatment).

**Table 4:** Quality assessment of trial reports included for review

Trial	Randomization		Blinding	Withdrawals	Intention to Treat Analysis
	Generation	Concealment			
Koonin <i>et al.</i> , 2001 <sup>92</sup> (Sheree Debbie Koonin, personal communication: 2003 Oct 02)	Inadequate	Inadequate	No	Yes	No
Mercer <i>et al.</i> , <sup>91</sup> 1999	Unclear	Unclear	No	No	No
Olafsdottir <i>et al.</i> , <sup>89</sup> 2001	Unclear	Adequate <sup>b</sup>	Parents and assessor <sup>a</sup>	Yes	Yes <sup>c</sup>
Wiberg <i>et al.</i> , <sup>90</sup> 1999	Unclear	Inadequate	Assessor	Yes	No

<sup>a</sup> The trial does not describe itself as double-blinded. <sup>b</sup> Based on supplementary information. <sup>c</sup> An intention-to-treat (ITT) analysis was performed, although the decision to analyze data using strict ITT did not appear in the methods section of the report and may have been conducted *post hoc*.

### 3.2.2 Critical review and synthesis of information

#### a) *Does spinal manipulation reduce the signs and symptoms of infantile colic?*

##### *Primary outcome*

Reduction in Symptoms of Infantile Colic (crying and fussing) (Table 5).

In the South African trial abstract by Mercer *et al.*,<sup>91</sup> it was unclear if crying and fussing were measured separately or together. Infantile colic behaviour was recorded by administering questionnaires to parents at each visit. An investigator blinded to the treatment allocation subsequently interpreted these. The number of hours of infantile colic behaviour before treatment or after one week of treatment was not reported. All that is known from the abstract is that “a statistically significant difference in the response to treatment by the experimental group as opposed to the placebo group” was detected. A resolution of symptoms was reported in 93% of the infants within two weeks in the treatment group, but a response rate in the comparator group was not reported. We were unsuccessful at corresponding with the authors to obtain clarification.

In the unpublished manuscript of the South African trial conducted by Koonin *et al.* (Sheree Debbie Koonin, personal communication: 2003 Oct 02), the duration of crying was established by means of a questionnaire. Just before treatment, the mean daily duration of crying (colic attack) reported for both treatment and control groups was 5.2 hours (95% CI: 4.4; 5.9) and 4.6 hours (95% CI: 3.9; 5.2) respectively. Crying was reduced to 0.13 hours (95% CI 0.03; 0.22) in the treatment group and 2.7 hours (95% CI:1.7; 3.7) in the control group after two weeks. Because questionnaires were administered after two weeks, the impact of treatment after one week was unknown.

In the Danish trial reported by Wiberg *et al.*,<sup>90</sup> crying and fussing behaviour were recorded using a validated parent diary.<sup>95</sup> A blinded investigator interpreted the diaries. One week before the start of treatment, infants allocated to counselling plus manipulation and counselling plus medication (dimethicone) treatment arms exhibited 4.3 (95% CI: 4.0; 4.6) and 5.2 (95% CI: 4.5; 5.9) hours respectively of colic behaviour per day on average. Just before treatment, infants in the counselling plus manipulation and counselling plus medication (dimethicone) treatment groups exhibited an average 3.9 hours (95% CI: 3.5; 4.3) and 3.4 hours (95% CI: 3.0; 3.8) of daily infantile colic behaviour respectively. Between days 8 and 11 after the start of treatment, the mean reduction in the average duration of daily colic was 2.7 hours (95% CI: 2.4; 3.0) and 1.0 hour (95% CI: 0.6; 1.4). The mean daily duration of colic was not reported but can be inferred to be roughly 1.2 hours and 2.4 hours (95% CIs cannot be calculated) in each trial arm. Precise estimates of the mean daily duration of colic were unavailable.

In the Norwegian trial,<sup>89</sup> parents were asked to keep a 24-hour diary of crying. It was unclear if the investigator interpreting the diaries was blinded from treatment allocation. When treatment was initiated, infants allocated to spinal manipulation exhibited an average duration of 5.1 hours (95% CI: 4.6; 5.6) of crying compared to 5.4 hours (95% CI: 4.8; 6.0) for those allocated to placebo. On day 8 of treatment, this was reduced to an average of 3.1 hours (95% CI: 2.7; 3.5) of crying per day in spinal manipulation recipients and 3.1 hours (95% CI: 2.6; 3.6) of crying per day in sham manipulation recipients.

**Table 5:** Mean change in duration of colic symptoms after one week in included trials

Trial	Treatment Allocation	Mean Duration of Daily Colic Before Treatment, Hours (95% CI)	Mean Duration of Daily Colic After One Week, Hours (95% CI)	Mean Change in Duration After One Week, Hours (95% CI)	Mean Duration of Daily Colic After Two Weeks, Hours (95% CI)	Statistical Test for Difference, Value
Koonin <i>et al.</i> , 2001 <sup>92</sup> (Sheree Debbie Koonin, personal communication: 2003 Oct 02)	Counselling + drug therapy + chiropractic care	5.2 (4.4 to 5.9)	NR	NR	0.13 (0.03 to 0.22)	Student-Newman-Keuls method (p<0.05)
	Counselling + drug therapy	4.6 (3.9 to 5.2)	NR	NR	2.7 (1.7 to 3.7)	
Mercer <i>et al.</i> , <sup>91</sup> South Africa, Abstract, 1999	Spinal manipulation	NR	NR	NR	NR	Mann-Whitney unpaired two-tailed test
	Placebo (non-functional ultrasound)					
Olafsdottir <i>et al.</i> , <sup>89</sup> Norway, Published, 2001	Spinal manipulation + counselling	5.1 (4.6 to 5.6)	3.1 (2.7 to 3.5)	NR	NA	Unpaired t test, p=0.982
	Sham manipulation + counselling	5.4 (4.8 to 6.0)	3.1 (2.6 to 3.6)	NR	NA	
Wiberg <i>et al.</i> , <sup>90</sup> Denmark, Published, 1999	Spinal manipulation + counseling	3.9 (3.5 to 4.3)	NR	2.7 (2.4 to 3.0)	NA	Unpaired t test, P=0.004
	Dimethicone + counseling	3.3 (3.0 to 3.8)	NR	1.0 (0.6 to 1.4)	NA	

NR=not reported; NA=data not available.

**b) Is spinal manipulation for infantile colic safe?**

None of the four controlled trial reports provided information about adverse events during treatment. Nothing was reported in any trial that suggested an adverse event had occurred even though it might not be labelled as such.

**Secondary outcomes**

Increases in sleep time, parental anxiety and quality of life and number of infants no longer fulfilling criteria for diagnosis were not reported outcomes in any of the trials. The South African abstract<sup>91</sup> reported complete resolution of symptoms in 93% of those treated with spinal manipulation, but it did not report resolution of symptoms in placebo recipients or the number of infants no longer fulfilling diagnostic criteria.



## 4 DISCUSSION

We identified four controlled clinical trial reports describing the manipulation of infants with colic. Three reported symptom duration in treatment and control groups, while none provided information about adverse events during treatment.

We conducted a systematic review, as this can minimize potential reviewer bias and lead to more reliable conclusions.<sup>78</sup> Few systematic reviews exist in pediatric complementary and alternative medicine.<sup>79</sup> Thus, we made every effort to conduct our review and report its results with the highest rigour.

We sought to draw conclusions from the evidence in light of its apparent methodological quality. We chose quality measures (Jadad scale, ITT analysis, allocation concealment) that were associated with exaggerated or unreliable reported effects from treatment when they were absent.<sup>96,97</sup> A potential weakness of our review was that the rules for interpretation of evidence or *a priori* sensitivity analyses based on these quality indicators were not stipulated in our protocol. Instead, interpretation was determined by consensus and peer review. None of the three trials demonstrated an impact on symptom duration in light of their methodological weaknesses.

All trial reports received Jadad scores of  $\leq 2$ . Compared with high-quality trials (score  $> 2$ ), low-quality trials (score  $\leq 2$ ) have been associated with an increased estimate of benefit.<sup>98,99</sup> In addition, both trials reporting a reduction in symptom duration<sup>90,92</sup> were judged to have inadequate concealment of the randomization order, which was associated with bias.<sup>100-103</sup>

Blinding (masking) trial participants is associated with less bias.<sup>96</sup> Although blinding is usually impractical in trials of manual therapy, infantile colic offers investigators a unique opportunity to reduce bias by blinding parents. The trial conducted by Olafsdottir *et al.*<sup>89</sup> may have more appropriately minimized the influence of bias by adequately concealing the randomization sequence<sup>100,101</sup> and blinding parents and assessors.<sup>102</sup> Concealment of treatment allocation in the Norwegian trial report is described only as “sealed envelopes.” Although this technique can reduce influence from trial investigators, it can be circumvented (e.g. if the envelopes are not opaque or serially numbered).<sup>101</sup> It is unclear from the text whether these measures were taken.

In addition to methodological weaknesses, other factors could have influenced the observed effect on symptoms. In one trial,<sup>90</sup> manipulated infants (and parents) received more attention (e.g. from the chiropractor conducting a case history and physical examination) than those in the self-medication arm. Added attention or reassurance given to parents during visits to the chiropractor could have influenced their perception of symptoms or influenced symptoms through parent-infant interaction. It was impossible to isolate the effect of manipulation alone. A well conducted trial of this design might be better suited to answer a question about the effectiveness of chiropractic treatment versus self-medication.

We also sought evidence of harm from the spinal manipulation of infants with colic,<sup>104</sup> but the presence or absence of adverse events is not described in any report. Deficiencies in adverse event reporting are well documented in trial reports.<sup>105</sup> Although well intended, seeking evidence of harm from controlled trials may have been too restrictive. We did conduct a search

post hoc for research evidence from observational studies and case reports. One report describes the incidence of side effects in infants treated with colic. In this four-week observational study involving 316 infants, no side effects are reported.<sup>85</sup> There are two case reports of serious complications associated with (but not necessarily caused by) the spinal manipulation of an infant.<sup>106,107</sup> It would be unrealistic to estimate the potential for harm from these limited data.

We did not find any other systematic reviews that addressed the questions posed in our objectives. Two reviews that examined the evidence regarding the effectiveness of chiropractic treatment on infantile colic, included three of the four trials from this review.<sup>108,109</sup> Neither review offered straightforward conclusions. Several explanations were presented to reconcile the seemingly contradictory results from identified trials.<sup>110,111</sup> These included a dose-response relationship (leading to positive results in trials with more frequent treatment) and a dilution of the specific treatment effect by counselling (leading to statistically insignificant results in the trials where counselling existed in both trial arms). Future empirical research should be conducted to test these assertions.

Our findings do not imply that spinal manipulation has no effect<sup>112</sup> on infants with colic or that it is unsafe. Instead, clinicians and patients must decide whether to manipulate infants based on their experiences, rather than the evidence from controlled clinical trials. There is no “gold standard” for treating infants with colic. The evidence has been shown to be similarly insufficient with respect to the use of alternative treatments for infantile colic.<sup>43-45</sup>

The need for better research is highlighted by the lack of conclusive findings from our review despite the identification of four trials. The objective of any intervention is to modify the natural history of a disease, to prevent or delay death or disability and to improve the health of the patient.<sup>113</sup> Because its symptoms are self-limiting<sup>114</sup> and because the course of colic plays itself over several months,<sup>36</sup> future researchers must try to recruit participants at an early age and to initiate the intervention promptly.

The importance of comparing infants of similar age cannot be underestimated. If a treatment group is older than a control group, the success of treatment could be exaggerated because infants are on the “down side” of the normal crying curve when the intervention is initiated or when the outcome is assessed. The reverse is true when infants are on the “up side” of the normal crying curve.

Investigators should make every effort to minimize the influence of potential sources of bias, as placebo response rates can be as high as 83%.<sup>115</sup> The randomization of infants (using a properly generated and concealed sequence) and the blinding of parents and assessors should be considered in future research. To study the specific effect of manipulation, a balance in the provision of care between treatment and control groups cannot be overemphasized. Well designed and rigorously conducted research could improve our understanding of this condition. It would also identify effective and ineffective strategies to minimize the potentially deleterious effects of infant colic.

## **5 CONCLUSIONS**

Despite the identification of four controlled clinical trials, there is no convincing evidence that spinal manipulation alone can affect the duration of infantile colic symptoms. The safety of spinal manipulation and its effect on sleep time, parental anxiety, number of colic diagnoses and quality of life could not be determined from the available evidence. More research must be conducted to adequately measure the safety and efficacy of spinal manipulation for the treatment of infantile colic.

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# Appendix 1: Databases Searched and Search Strategies

## Electronic Databases on DIALOG® Online Search System

Dissertation Abstracts Online (File 35)  
 MEDLINE® (File 154)  
 (1966 – 2002 May W3)  
 EMBASE® (File 73)  
 (1974 – 2002 May W3)  
 BIOSIS Previews® (File 55)  
 (1969 – 2002 May W3)  
 Alternative and Complementary  
 Medicine™ (AMED) (File 164)  
 (1984 – 2002 May)  
 MANTIS™ (File 91)  
 (1880 – 2002 Jun)  
 SPORTDiscus (File 48)  
 (1962 - 2002 Jun)  
 ExtraMED™ (File 467)  
 (2000 Dec)  
 PASCAL (File 144)  
 (1973 – 2002 Jun W1)  
 PsycINFO® (File 11)  
 (1887 – 2002 May W2)

### Legend for Search Syntax:

!	Explode the search term. Retrieve the search concept plus all narrower related terms.
?	Truncation symbol, one character only.
*	Truncation symbol, any number of characters.
()	Proximity operator. Words must be adjacent.
N	Proximity operator (terms are near to each other, in any order).
#N	Proximity operators (terms are near to other within specified number of words)
near	Proximity operator (terms are near to each other, in any order).
Next	Proximity operator. Words must be adjacent.
“ “	Search phrases.
ti	Search in record title.
ab	Search in record abstract.
de	Descriptor.
ME	Medical subject heading.
MeSH	Medical subject heading.
RD	Remove duplicates.

## DIALOG® Search Strategy

DIALOG® OneSearch performed on the above databases using the following search strategy.

1. Chiropractic/de OR Manipulative Therapies!/de
2. Manipulation, Spinal!/de OR Manipulation, Chiropractic/de OR Manipulation, Osteopathic/de
3. Manipulation, Orthopedic/de
4. Manipulative Medicine!/de OR Manipulative Therapies/de OR Musculoskeletal Manipulations!/de OR Spinal Manipulation/de OR Osteopathic Medicine/de
5. Spinal()manipulat?/ti,ab OR Chiropractic?/ti,ab OR Chiropractic()manipulat?/ti,ab or Manipulat?()therap?/ti,ab
6. Spinal()adjustment?/ti,ab OR Cervial()manipulat?/ti,ab OR Chiropractic()correction?/ti,ab
7. Chiropractic()adjustment?/ti,ab OR Manipulat?(2N)Spine?/ti,ab OR Toggle()recoil/ti,ab OR Manual?(3N)manipulat?/ti,ab OR Spinal()Manual()Therap?/ti,ab OR Spinal()care/ti,ab OR Springing(3N)spine?/ti,ab OR Reliev?(2N)subluxat?/ti,ab
8. Spine?(3N)manipulat?/ti,ab OR Manipulat?()treatment?/ti,ab
9. S1:S8 (*add sets 1 to 8*)
10. Colic/de OR Colic/ti,ab OR Colics/ti,ab OR Colicky/ti,ab
11. ((Crying/ti,ab OR Crying/de) AND (Excessive?/ti,ab OR Persistent?/ti,ab OR Prolonged/ti,ab))
12. Irritable()infant?/ti,ab OR Infant?(3N)fuss?/ti,ab OR Infant()Colic()Syndrome?/ti,ab

13. ((Stomach?/ti,ab OR Abdom?/ti,ab OR Tumm?/ti,ab OR Belly?/ti,ab) AND (Pain?/ti,ab OR Ache?/ti,ab OR Pain/de OR Sore?/ti,ab OR Discomfort?/ti,ab OR Distress?/ti,ab OR Cramp?/ti,ab))
14. Abdominal Pain/de
15. S10:S14 (*add sets 10 to 14*)
16. S9 AND S15
17. Human? OR People? OR Person?
18. S16 AND S17
19. RD S18

*Total hits = 181 references*

*MEDLINE<sup>®</sup> = 26 unique references*

*EMBASE<sup>®</sup> = 27 unique references*

*MANTIS<sup>™</sup> = 112 unique references*

*BIOSIS Previews<sup>®</sup> = 4 unique references*

*Disseration Abstracts Online = 1 unique reference.*

*Allied and Complementary Medicine<sup>™</sup> = 11 unique references*

*Search performed May 24, 2002. Regular alerts set up on DIALOG<sup>®</sup> until April 2003.*

### **Electronic Database on CD-ROM**

The Cochrane Library, Issues 2 & 3, 2002 and updates on Issues 1 & 2, 2003

1. Chiropractic\*:ME OR Manipulation-Spinal\*:ME OR Manipulation-Orthopedic\*:ME
2. (Manipulat\* near Therap\*)
3. (Spinal near Manipulat\*)
4. (Manipulat\* near Spine)
5. (Spinal near Adjustment\*)
6. (Chiropractic near Correction)
7. (Chiropractic near Adjustment\*)
8. ( Manual near Manipulat\*)
9. (Toggle next Coil)
10. (Toggle near Recoil)
11. (Spinal next Care)
12. (Springing near Spine)
13. (Reliev\* near Subluxation\*)

14. (Manipulat\* near Treatment\*)
15. Colic\*:ME
16. (Irritable near Infant\*)
17. (Infant\* near Fuss\*)
18. (Persistent near Crying)
19. (Excessive near Crying)
20. (Prolonged and Crying)
21. (Inconsolable near Crying)
22. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14
23. #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21
24. #22 AND #23

*Search performed May 24, 2002*

*The Cochrane Controlled Trials Register = 4 references*

### **Online Database on CINAHLdirect<sup>®</sup> Online Service**

CINAHL<sup>®</sup> (1982 – 2002)

Chiropractic Manipulation/de OR  
Chiropractic Assessment/de OR  
Manipulation, Osteopathy/de OR  
Manipulation, Orthopedic/de OR  
Manual Therapy/de

Appropriate keywords were used to mirror the DIALOG<sup>®</sup> search. Appropriate search syntax for CINAHLdirect<sup>®</sup> Online Service used.

*Search performed May 24, 2002*

*Total hits = 8 references*

### **Online Database on the Internet by The Chiropractic Library Consortium (CLIBCON)**

Index to Chiropractic Literature (1985 – 2002)  
Manipulation, Chiropractic/de OR  
Manipulation, Spinal/de OR  
Manipulation, Orthopedic/de OR  
Chiropractic/de AND

Crying/de OR Colic/de OR Abdominal Pain/de

Appropriate keywords were used to mirror the DIALOG® search.

*Search performed May 24, 2002  
Total hits = 11 references*

### **Online Database on the Internet by the National Library of Medicine**

PubMed  
(1966 – May 2002)

1. Manipulation, Spinal [MeSH]
2. Manipulation, Orthopedic [MeSH]
3. Chiropractic [MeSH]
4. Manipulation, Osteopathic [MeSH]
5. Manipulative Therapy [Title/Abstract]
6. Chiropractic Adjustment\* [Title/Abstract]
7. Spinal Manipulation [Title/Abstract]
8. Reliev\* Subluxation\* [Title/Abstract]
9. Osteopathic Manipulation\* [Title/Abstract]
10. Orthopedic Manipulation\* [Title/Abstract]
11. Toggle coil [Title/Abstract]
12. Toggle recoil [Title/Abstract]
13. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12
14. Colic [MeSH]
15. Abdominal Pain [MeSH]
16. Irritable infant\* [Title/Abstract]
17. Infant\* fuss\* [Title/Abstract]
18. Inconsolable crying [Title/Abstract]
19. Reliev\* subluxation\* [Title/Abstract]
20. Excessive crying [Title/Abstract]
21. Persistent crying [Title/Abstract]
22. Prolonged crying [Title/Abstract]
23. #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
24. #13 AND #23

*Search performed May 23, 2002  
Total # of hits = 14 references.*

*PubMed updates performed every two months until April 2003.*

### **Online Database by the Research Council for Complementary Medicine, UK**

©The Centralized Information Service for Complementary Medicine (CISCOM) database  
(1981 – 1998)

Search performed by RCCM staff  
Keywords from DIALOG® search supplied by CCOHTA staff.

*Total # of hits = 8 references*

*Grey literature was obtained by contacting experts as well as searching websites/databases of HTA and related agencies, trial registries, major pediatric and chiropractic associations.*

## Appendix 2: Outcomes for Data Abstraction

### Study Characteristics

Year of publication  
Language of publication  
Country  
Publication status  
Funding source  
Journal indexed (yes or no)  
Author qualifications  
Sample size (total and by group)  
Design (RCT parallel, RCT cross-over, historic control, concurrent control, other)  
Criteria for diagnosis of colic  
Who diagnosed colic  
When was colic diagnosed (age)  
Length of study  
Length of follow up after last treatment  
Intent-to-treat analysis

**Treatment Information:** Data will be collected for both groups separately.

Treatment details  
Number of treatments  
Frequency of treatments  
Treatments during periods of crying or fussing (yes or no)

**Study Population:** Data will be collected for both groups separately.

Birth:  
    Length of gestation  
    Type of delivery (vaginal spontaneous, vaginal induced, c-section elective, c-section urgent)  
    Position: breech, cephalic  
Family information:  
    Birth order (% first born)  
    Family structure  
    Socioeconomic status  
    Support  
    Coping mechanisms  
    Family history  
Sex (% male, % female)  
Age  
Age at diagnosis  
Age at first treatment  
Previous treatments  
Concurrent treatments  
General health

Feeding

Breast versus bottle, formula versus breast milk

Type of formula (soy versus cow's milk based)

**Outcomes:** Data will be collected for both groups separately.

Method of assessment

Crying time

Baseline (SD)

Endpoint (SD)

Mean change

Fussing time

Baseline (SD)

Endpoint (SD)

Mean change

Combined crying and fussing time

Baseline (SD)

Endpoint (SD)

Mean change

Number no longer meeting criteria for colic

Sleep time

Baseline (SD)

Endpoint (SD)

Mean change

Family function:

Parental anxiety

Parental quality of life

Sibling anxiety

Sibling quality of life

Adverse events (open comment or text box)

- Detailed tables of data, i.e. tabulated trial evidence
- Step-by-step details of analyses, e.g., cost utility analysis
- Copies of data collection forms, questionnaires, instruments

## Appendix 3: Reviewer Quality Assessment Forms

### Jadad Scale

RM # \_\_\_\_\_ Reviewer \_\_\_\_\_

Randomization: Total points:  0  1  2

A trial reporting that it is “randomized” receives one point. Trials describing an appropriate method of randomization (table of random numbers, computer generated) receive an additional point. If the report describes the trial as randomized and uses an inappropriate method of randomization (date of birth, hospital numbers) a point is deducted.

Double-blinding: Total points:  0  1  2

A trial reporting that it is “double-blind” receives one point. Trials that describe an appropriate method of double-blinding (identical placebo, active placebo) receive an additional point. If the report describes the trial as double-blind and uses an inappropriate method (e.g., comparison of tablets versus injection with no double dummy), a point is deducted.

Withdrawals and drop-outs: Total points:  0  1

A trial reporting the number and reason for withdrawals receives one point. If there is no statement, no point is given.

Total score  low (0 to 2 points)  moderate (3 to 4 points)  high (5 points)

### Allocation concealment

Adequate: Central randomization; numbered or coded bottles or containers; drugs prepared by a pharmacy; serially numbered, opaque, sealed envelopes

Inadequate: Alternation; reference to case record number or date of birth

Unclear: Allocation concealment approach is not reported or fits neither of the above categories.

Was treatment allocation concealed for investigators?

adequate  inadequate  unclear



## **Appendix 4: Excluded Retrieved Reports with Reasons**

### **Excluded – Basic Science Studies**

- Wagner LC. Respiratory allergies. *J Am Osteopath Assoc* 1950;49(9):481-3.
- King ND. Gastrointestinal allergies in pediatrics. *J Am Osteopath Assoc* 1950;49(9):479-80.
- Davidson D. Intestinal obstruction. *J Am Osteopath Assoc* 1956;55(12):755-7.
- Lavet NO. Pediatric anorectal disorders. *J Am Osteopath Assoc* 1956;56(4):270-4.
- Spitzer IE. Acute abdominal pain in children: important consideration in diagnosis. *J Am Osteopath Assoc* 1980;80(3):195-8.
- Beal MC. Viscerosomatic reflexes: a review. *J Am Osteopath Assoc* 1985;85(12):786-801.
- Rucco V, Genco F. Terapia manipolativa vertebrale e patologia viscerale [Manipulative vertebral therapy and visceral pathology]. *Riabilitazione* 1994;27(4):229-45.
- Pistolese RA. Risk assessment of neurological and/or vertebrobasilar complications in the pediatric chiropractic patient. *J Vert Subluxation Res* 1998;2(2):77-85.
- Robertson S. Neuroanatomical review of visceral pain. *J Man Manipulative Ther* 1999;7(3):131-40.
- Blom L, Møholt K, Istre O, Bondesen H. Fødselsmådens betydning for senere udvikling af spædbarnskolik. *Ugeskr Laeger* 1988;150(30):1847-9.
- Matheson I, Kristensen K, Lunde PK. Spædbarns plager og legemiddelbruk. Hvilken betydning har amming? *Tidsskr Nor Lægeforen* 1989;109(22):2123-8.

### **Excluded – Case Reports**

- Sheader WE. Chiropractic management of an infant experiencing breastfeeding difficulties and colic: a case study. *J Clin Chiropractic Pediatr* 1999;4(1):245-7.
- Gutmann G. Das atlas-blockierung-syndrom des säuglings und des kleinkindes. *Manuelle Med* 1987;25:5-10.

### **Excluded – Commentaries**

- Nilsson N. Infant colic and chiropractic. *Eur J Chiropractic* 1985;33(4):264-5.

Klug BH. Behandling af spædbarnskolik: en kritisk kommentar. *Manedsskr Prakt Laegegern* 1991;69:275-6.

Margolius FR. Compared with dimethicone, 2 weeks of spinal manipulation reduced infantile colic behaviour at 4-11 days after initial treatment [commentary on Wiberg JMM, Nordsteen J, Nilsson N. The short-term effect of spinal manipulation in the treatment of infantile colic: a randomized controlled clinical trial with a blinded observer. *J Manipulative Physiol Ther* 1999 Oct;22(8):517-22]. *Evidence-Based Nurs* 2000;3(2):42.

Walker ML. Chiropractic spinal manipulation did not lead to an improvement in infantile colic or reduce crying [commentary on Olafsdottir E, Forshei S, Fluge G, et al. Randomised controlled trial of infantile colic treated with chiropractic spinal manipulation. *Arch Dis Child* 2001 Feb;84(2):138-41]. *Evidence-Based Nursing* 2001;4(3):76-7.

Ernst E. Spinal manipulation = placebo? *Focus Alternat Complement Ther* 2001;6(3):202-3.

### **Excluded – Duplicates**

Olafsdottir E, Forshei S, Fluge G, Markestad T. Infantile colic treated with chiropractic spinal manipulation [abstract]. *J Pediatr Gastroenterol Nutr* 2000;31 Suppl 2:S174.

### **Excluded – Epidemiological (Surveys or Natural History) Studies**

Dehlholm J, Mahneke T, Mortensen H, Rasmussen PB. Amning. Med relation til en spørgeskemaundersøgelse blandt mødre, som netop har født. *Manedsskr Prakt Laegegern* 1978;56(2):65-82.

Buchman J, Bülow B. Funktionell Kopfgelenksstørungen bei Neugeborenen in Zusammenhang mit Lagereaktionsvergalten und Tonusasymmetrie [Functional disturbances of the upper cervical spine in newborns]. *Manuelle Med* 1983;21:59-62.

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Moesgaard Jensen K, Rasmussen LR. Children in Danish chiropractic clinics: a descriptive questionnaire study. *Eur J Chiropractic* 1989;37(4):117-24.

Durant CL, Verhoef MJ, Conway PJ, Sauve RS. Chiropractic treatment of patients younger than 18 years of age: frequency, patterns and chiropractors' beliefs. *Paediatr Child Health* 2001;6(7):433-8.

Wiberg JM, Nilsson N. Infants with colic may have had a faster delivery: a short, preliminary report. *J Manipulative Physiol Ther* 2000;23(3):208-10.

Spigelblatt L, Laine-Ammara G, Pless IB, Guyver A. The use of alternative medicine by children. *Pediatrics* 1994;94(6 I):811-4.

### **Excluded - Letters**

Hansen KC. Spædbørnskolik og kiropaktorbehandling. Korrespondance med svar af Søren K Sørensen. *Ugeskr Laeger* 1984;146(15):1176.

Frimodt-Møller N. Kiropaktorbehandling af born i forste levear [Chiropractic treatment of infants in the first year of life]. *Ugeskr Laeger* 1988;150(39):2355-6.

Charlton K, Klougart N. Infantile colic treated by chiropractors: a prospective study of 316 cases [letters]. *J Manipulative Physiol Ther* 1990;13(5):288.

Volkening DA. The short-term effect of spinal manipulation in the treatment of infantile colic a randomized controlled clinical trial with a blinded observer... [comment on: Wiberg JM, Nordsteen J, Nielsson N. The short-term effect of spinal manipulation in the treatment of infantile colic: a randomized controlled clinical trial with a blinded observer. *J Manipulative Physiol Ther* 1999;22:517-22]. *J Manipulative Physiol Ther* 2000;23(5):365.

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### **Excluded – News Items**

Chapman-Smith D. Infantile colic, medical tunnel vision and the art of chiropractic. *J Chiropractic* 1989;26:22-5.

Colic could be spinal dysfunction. *Today's Chiropractic* 1992;21(6):13.

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### **Excluded – Observational Studies**

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### **Excluded – Overviews**

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Krasilnikoff PA. Kiropraktorbehandling af spaedbarnskolik [Chiropractor treatment of infantile colic]. *Ugeskr Laeger* 1988;150(30):1823-4.

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Rasmussen LB. Kolikbørn kan hjælpes: de skal ha' nogen BANK! *Vores Børn* 1991;3:10-2.

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### **Excluded – Reviews**

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### **Excluded – Unrelated Intervention**

Danielsson B, Hwang P. Vibroakustisk behandling vid spædbarnskolik saknar effekt. *Läkartidningen* 1989;86(21):1985-6.

Kobrossi T, Steiman I. Thermographic investigation of viscerogenic pain: a case report. *J Can Chiropractic Assoc* 1990;34(3):125-30.

### **Excluded – Unrelated Patient Group**

Kondzielle W. Unklarer Abdominalschmerz - Psoashartspann und seine Behandlung. *Erfahrungsheilkunde* 1986;35(5):352-7.

Davydov O, V. Effektivnost' manual'noi terapii pri kardial'nom i abdominal 'nom pozvonochnykh sindromakh [The efficacy of manual therapy in cardiac and abdominal spinal syndromes]. *Voenn Med Zh* 1998;319(6):43-5.