

Safety of Chiropractic Interventions

A Systematic Review

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Study Design. Systematic review of reported adverse events.

Objective. To evaluate the tolerability and safety of chiropractic procedures.

Summary of Background Data. Despite the increasing popularity of chiropractic, there are few properly designed prospective controlled trials, and there is a disproportionate lack of evaluation of its safety profile. The literature reports multiple neurologic complications of spinal manipulation, some of which are clinically relevant and even life threatening.

Methods. We performed an electronic search in 2 databases: Pubmed and the Cochrane Library for the years 1966 to 2007. All articles that reported adverse reactions associated with chiropractic were included irrespective of type of design. The outcome measures were the type of adverse events associated or attributed to chiropractic interventions and their frequency.

Results. A total of 376 potential relevant articles were identified, 330 of which were discarded after abstract or complete article analysis. The search identified 46 articles that included data concerning adverse events: 1 randomized controlled trial, 2 case-control studies, 7 prospective studies, 12 surveys, 3 retrospective studies, and 115 case reports.

Most of the adverse events reported were benign and transitory, however, there are reports of complications that were life threatening, such as arterial dissection, myelopathy, vertebral disc extrusion, and epidural hematoma. The frequency of adverse events varied between 33% and 60.9%, and the frequency of serious adverse events varied between 5 strokes/100,000 manipulations to 1.46 serious adverse events/10,000,000 manipulations and 2.68 deaths/10,000,000 manipulations.

Conclusion. There is no robust data concerning the incidence or prevalence of adverse reactions after chiropractic. Further investigations are urgently needed to assess definite conclusions regarding this issue.

Key words: spinal manipulation, chiropractic, adverse events, safety. **Spine 2009;34:E405–E413**

the diagnosis, treatment, and prevention of disorders of the neuromusculoskeletal system and the effects of these disorders on general health. WHO published guidelines focused on basic chiropractic training and the serious adverse reactions that can occur when safety issues are not respected. No information is reported about chiropractic efficacy. (The WHO definition, WHO, Guidelines on Chiropractic, 2005).²

Although the multiple definitions of chiropractic are unclear in the discrimination of the type of therapeutic procedures included in this treatment, the 2 main types of therapeutic interventions are: manipulation (high velocity, low amplitude thrusts that cannot be resisted by the patient) and mobilization (low-velocity passive motion that can be stopped by the patient).³

Although the list of indications for which chiropractic is recommended is enormous, there is insufficient published evidence to support or refuse the efficacy of this treatment modality.^{4,5} Recent reviews about its effectiveness in multiple indications concluded that the efficacy of spinal manipulation was not demonstrated for the treatment of any condition,⁶ and that there were few properly designed randomized controlled trials, such that the results were frequently inconclusive.^{7–10} On the other hand, because it does not constitute a pharmacological intervention and is considered a nonconventional therapy, it has not been subjected to formal efficacy and safety evaluations demanded by the national drug agencies.

Without a robust demonstration of effectiveness, and a disproportional overgrowth of popularity, the evaluation of the safety profile gains more relevance. Reinforcing this need, the literature reports multiple cases of patients who experienced serious adverse neurologic events after chiropractic manipulations.^{11–31} The aim of this systematic review was to identify and appraise all studies specifically designed to evaluate safety data concerning adverse events associated with chiropractic practice.

Materials and Methods

Study Identification

We performed an electronic search in 2 databases: Pubmed and the Cochrane Library for the years 1966 to 2007. The key words used were: chiropractic, adverse reactions, adverse events, safety, and spinal manipulation. The search had no language restrictions, and we followed the approach presented in Appendix 1. We selected data regarding spinal manipulation safety. Additional references were identified from the bibliographies of published articles that were relevant to the topic of spinal manipulation. We also analyzed all articles that reported adverse reactions related to spinal manipulation in the form of case series or case reports. Abstracts and other presentation formats were also included.

Since the 19th century, chiropractic procedures have been applied to treat a vast number of conditions.¹ The World Health Organization (WHO) has recently defined chiropractic as a health care profession concerned with

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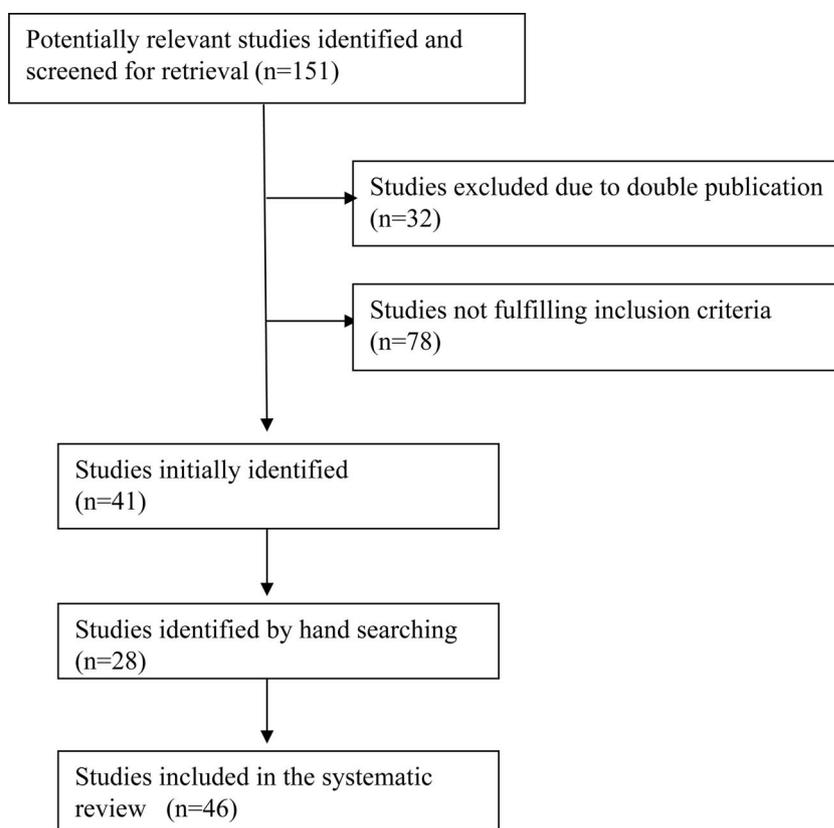


Figure 1. Diagram showing the search results.

Study Selection

Two independent reviewers (L.G., P.C.) screened titles and abstracts of studies identified by the literature search for eligibility. We included in this systematic review all articles that reported adverse reactions associated with chiropractic irrespective of type of design. The definition of an adverse event was based on each author judgment. The outcome measures for this review were the type of adverse events associated with or attributed to chiropractic interventions and their frequency (as shown by percentage of subjects). The definition of an adverse event and the causality relationship with the chiropractic intervention was based on the judgment of the authors of each study. This evaluation was limited to the safety profile of chiropractic; therefore, clinical efficacy, the burden of disease, prevalence, epidemiology, cost, and other variables not directly related to safety were not included in the study selection, data extraction, and assessment. Disagreements were resolved by consensus. It was only possible to conduct a descriptive meta-analysis because of the studies design and outcomes reported.

Data Extraction

Data extraction was performed by one author (L.G.) and over-read by a second author (J.F.). Disagreements were resolved by consensus. Extracted information included type of design, type of intervention, number of patients, and type and number of adverse reactions.

Results

A total of 151 potentially relevant articles were identified, 110 of which were discarded after abstract or complete article analysis, either due to adverse reactions reported in patients with an underlying disease that predisposed them to complications related to chiropractic [osteogenesis im-

perfect,³² expansive vertebral hemangioma,³³ osteoporotic fracture³⁴], and/or articles corresponded to double publication³² among other various reasons. Hand searches identified an additional 28 articles (Figure 1).

The search identified 46 articles, which included data concerning adverse events:

- One randomized controlled trial^{35,36};
- Two case-control studies^{37,38};
- Six prospective studies³⁹⁻⁴⁴;
- Twelve surveys⁴⁵⁻⁵⁶;
- Three retrospective studies⁵⁷⁻⁵⁹; and
- Hundred case reports.^{11-29,57,60-67}

Randomized Controlled Trials

The only randomized controlled trial is summarized in Table 1. It was conducted in 4 Southern California health care clinics with the objective to document the types and frequencies of adverse reactions related to chiropractic treatments. Results concluded that 30% of respondents reported at least 1 adverse event, most commonly increased pain and headache. Patients randomized to manipulation were more likely (not reaching clinical significance) than those randomized to mobilization to report an adverse reaction (adjusted OR = 1.44, 95% CI = 0.85, 2.43). No serious adverse events were reported.^{35,36}

Case-Control Studies

There were 2 identified case-control studies. A population-based case-control study was conducted in Canada

Table 1. Randomized Controlled Trials

Author Yr	Inclusion Criteria	Exclusion Criteria	Interventions	Study Design	Randomization	No. Patients	Follow-up	Primary Outcome	Other Outcomes	Results
Hurwitz et al ^{35,36*}	Neck pain 18- to 70-yr-old	Neck pain secondary to other underlying disease Progressive neurological deficit Severe coexisting disease Treatment by electrical devices Blood coagulation disorder Treatment with corticosteroids or anticoagulant medications History of stroke or transient ischemic attacks	Manipulation with and without heat vs. Manipulation with and without electrical muscle stimulation vs. Mobilization with and without heat vs. Mobilization with and without electrical muscle stimulation	Balanced 2 × 2 factorial design	Sealed envelopes	Manipulation: 171 Mobilization: 165 336 patients were enrolled and 280 (83%) responded to the adverse event questionnaire	6 mo	Mailed questionnaire about possible adverse reactions For each reported symptom, subjects were asked to rate the amount of discomfort on a 0–10 numerical rating scale: how long after the treatment it began, how long it lasted, and how much it affected their normal daily activities at home or work	Neck pain intensity (0–10 numerical rating scale) Neck disability index Expectation of treatment success (0–10 numerical rating scale)	30% reported at least 1 adverse symptom Most frequent adverse event: increased neck pain or stiffness Increased risk of adverse reaction with manipulation (OR = 1.44, CI = 0.83–2.49)

*Hurwitz published 2 articles regarding the same study: one³⁹ in which the objective was to compare the relative effects of cervical spine manipulation and mobilization on adverse reactions and to estimate the effects of adverse reactions on satisfaction and clinical outcomes among patients with neck pain; in the other article,³⁸ the objective was to document the types and frequencies of adverse reactions associated with the most common chiropractic treatments for neck pain, and to identify possible clinical predictors of adverse reactions to chiropractic treatment.

using 582 cases of vertebrobasilar accidents (VBA), each of which was matched with 4 patients without a history of stroke. In those aged <45 years, VBA were 5 times more likely than controls to have visited the chiropractor within 1 week of the VBA (OR: 5.03; 95% CI from bootstrapping: 1.32–43.87) and 5 times more likely to have made more than 3 visits for cervical treatment in the preceding month (OR: 4.98; 95% CI from bootstrapping: 1.34–18.57). There were no significant associations for patients over 45 years of age.³⁷

Using a nested case-control design, all patients under age 60 with cervical arterial dissection (n = 151) and ischemic stroke and TIA were reviewed and matched with 306 controls. In a multivariate analysis, vertebral artery dissections were independently associated with spinal manipulative therapy within 30 days (OR: 6.62, 95% CI: 1.4–30) and pain before stroke/TIA (OR: 3.76, 95% CI: 1.3–11), even after controlling for neck pain.³⁸

Prospective Cohorts

Table 2 summarizes the data collected from 6 prospective studies published in the literature. All of these studies used questionnaires in their methodology in which the interview was conducted by physiotherapists,³⁹ chiropractors,^{40–42} or questionnaires that were answered by the patients themselves.^{43,44} Except the study from Rivett and Milburn, a high rate of reported adverse events was observed ranging from 44% to 60.9%; most were characterized by local discomfort, exacerbation of pain, and radiation and headaches. These symptoms occurred most commonly in the first 24 hours after manipulation, were transient, mild, and benign. No serious adverse effects were reported.

Retrospective Cohorts

As already mentioned, there were 12 surveys published (Table 3) that involved neurologists and chiropractors as

well as other physicians from different countries. In most of the series, serious adverse events were reported totaling 308 cases: 163 strokes, 26 myelopathies, 100 radiculopathies, 3 transitory ischemic accidents, 1 acute subdural hematoma, and 29 other cases not specified. Minor adverse reactions were more common totaling 1337 cases (most of them were vertigo [1218] and diminishment or loss of consciousness⁴³). Most of these adverse events occurred within 24 hours after spinal manipulation. Five patients died and 80 were left with permanent neurologic deficits (in some patients the outcome was not stated). As we can see in Table 3, the incidence of neurologic complications is variable, varying from 5 strokes/100,000 manipulations to 1.46 case serious adverse events/10,000,000 manipulations. It was reported that 2.68 deaths/10,000,000 manipulations occurred.

There were 3 retrospective studies identified. Eighteen patients who presented to a neurosurgical practice were reviewed during a 6-year period who suffered a qualitative worsening of symptoms immediately after spinal manipulative treatment. Injuries resulted in spinal cord injury (including myelopathy, tetraparesis, central cord syndrome, or paraparesis) in 9 patients, cauda equina syndrome in 2 patients, and radiculopathy in 6 patients. Eighty-nine percent required surgery. Outcome was excellent in 50% and good in 37.5%. Three patients died from unrecognized malignancies.⁵⁷

A 5-year retrospective study reported the types of complications documented in a single group practice of 6 neurosurgeons. Complications of cervical spine manipulation therapy included radiculopathy (21 cases), myelopathy (11 cases), Brown-Séquard syndrome (2 cases), and vertebral artery occlusion (1 case). Twenty-one patients underwent surgery. Poor outcomes were observed in 3, outcome was unchanged in 1, and 17 improved.⁵⁸

Table 2. Prospective Investigations of the Safety of Spinal Manipulation, 1996 to 2004

Author, Yr	No. Practitioners	No. Interventions	No. Patients	Reporting Period	Type of Intervention	Evaluation Method	Nonparticipation and Missing Data	Results
Rivett and Milburn ³⁹	9 New Zealand physiotherapists	476	238	3 mo	Cervical spine manipulation defined as small amplitude thrust technique that is too rapid for the patient to control or prevent, applied to the spine anywhere between the atlanto-occipital (0–C1) and cervicothoracic (C7–T1) joints	Adverse events form completed by physiotherapists	20 physiotherapists were approached and only 9 returned forms, of whom only 1 participated for 3 wk	1 adverse event (exacerbation of neck pain during 24 h). Incidence of complications: 1/50,000 a 2/5,000,000 manipulations
Senstad <i>et al</i> ⁴⁰	10 Norwegian chiropractors	368	95	10 consecutive patients, up to a maximum of 6 visits	Spinal manipulative therapy	Questionnaire completed by chiropractors	5% of patients were lost for follow-up	One-third reported side effects 23% local or radiating symptoms 90% moderate or slight 87% commenced on the day of therapy 83% disappeared within 24 h
Leboeuf-Yde <i>et al</i> ⁴¹	66 Swedish chiropractors	1858	625	10 consecutive patients per chiropractor 6 mo	Spinal manipulative therapy	Questionnaire completed by chiropractors	86 were approached and only 66 participated 27% of target sample of patients did not participate 5% of patients were lost for follow-up	44% reported adverse reactions in the area of treatment 68% moderate or slight 58% commenced on the day of therapy 34% disappeared within 24 h
Senstad <i>et al</i> ⁴²	102 Norwegian chiropractors	4712	1058	12 consecutive new patients until a maximum of 6 visits	Spinal manipulative therapy	Questionnaire completed by chiropractors	146 were approached and only 102 participated 3.5% of patients only returned once 38% of patients returned 6 times	55% reported adverse reactions 53% local discomfort 85% moderate or slight 64% appeared within 4 h of treatment 74% disappeared within 24 h
Barrett <i>et al</i> ⁴³	9 British chiropractors	68	68	12 consecutive new patients	Spinal manipulation (to one or more areas of the spine)	Questionnaire completed by patients	11 were approached and only 9 participated 74% of patients responded of which only 63% forms were complete	53% reported adverse reactions 82% extra and radiating pain 2.3 (95% CI: 2–2.64) severity of reactions (1 = hardly any, 5 = worst possible) 44.4% appeared within 1 h of treatment
Cagnie <i>et al</i> ⁴⁴	59 Belgian manipulative therapists (20 physiotherapists, 18 osteopaths and 21 chiropractors)	930	465	15 consecutive new patients 4 mo	Spinal manipulation	Questionnaire completed by patients	50 manipulative therapists were approached and only 20 physiotherapists, 18 osteopaths and 21 chiropractors participated 51 participating practitioners returned their questionnaires 639 questionnaires were distributed (83.5% of the optimal number) and 465 patients returned their questionnaires (72.8%)	60.9% reported adverse reactions 54.5% headache, stiffness, local discomfort 60.5% appeared within 4 h of treatment 64% disappeared within 24 h

Another study retrospectively reviewed 64 medical-legal cases of strokes temporally associated with cervical spine manipulation. Ninety-two percent of cases presented with a history of head and/or neck pain and 16 (25%) cases presented with sudden onset of new and unusual headache and neck pain often associated with other neurologic symptoms that may represent a dissection in progress. The strokes occurred at any point during the course of treatment and there was no apparent dose-response relationship to these complications (it occurred after the first or after multiple manipulations).⁵⁹ One hypothesis postulated by the authors is that there could be a dissection in progress before manipulation.

■ Case Reports

Regarding case reports, we identified 115 cases reported during 1925 to 2006. Most were strokes (66 cases)^{6,11,16,20,22,24,27–29,66,67}; there were 5 cases of spinal fluid leak presented as intracranial hypotension^{6,17,21,23,25}; 7 cases of spinal epidural hematoma^{6,11,18,26,65}; 2 cases of *cauda equina* syndrome^{14,37}; 20 of cases of herniated disc^{6,61,64}; 7 cases of radiculopathy^{19,58,62}; 3 cases of myelopathy^{4,58}; 3 cases of diaphragmatic palsy⁶; and 2 pathologic fractures of vertebra.^{15,61} We were only able to perform a descriptive analysis of the results due to the heterogeneity of the studies design and outcome reports of the data.

Table 3. Retrospective Studies Reporting Serious Adverse Events Associated With Spinal Manipulation

Author Yr	Population	Design	Type of Intervention	Evaluation Method	Reporting Period	Nonparticipation and Missing Data	Results
Gutmann ⁵¹	55 members of the Germany Society for Manual Medicine	Survey	Spinal manipulation	Questionnaire	Over professional careers	Not stated	1–3 cases/1,000,000 manipulations 30 minor adverse events in 30 patients: 10 vertigo; 20 diminished or loss of consciousness 7 major adverse events: 7 strokes 2 deaths, 3 with permanent neurological deficits
Dvorak ⁵²	203 members of the Swiss Society for Manual Medicine: 128 general practitioners; 28 rheumatologists; 21 internists; 14 orthopedic surgeons; 11 surgeons; 1 neurologist	Survey	Spinal manipulation	Questionnaire	Over professional careers	367 members of the Swiss Society for Manual Medicine were approached, only 203 participated	1255 minor adverse events: 1218 vertigo; 10 diminished consciousness; 12 loss of consciousness; 4 diminished or loss of consciousness with additional neurological symptoms; 11 radicular deficits 1 case/383,750 manipulations
Michaeli ⁵⁰	153 South Africa physiotherapists	Mail questionnaire	Spinal manipulation	Questionnaire	18 yr (1971–1989)	250 physiotherapists were approached, only 153 participated	52 minor adverse events in 29 patients: 12 dizziness; 11 nausea; 10 severe headache; 3 nystagmus; 3 blurring of vision, 3 vomiting; 3 brachialgia; 1 brachialgia with neurological deficit, 1 loss of consciousness; 1 acute wry neck full recovery in all patients
Carey ⁵⁵		Review of the reported legal/insurance claims Calculate the no. manipulations performed by chiropractors from Government Health Plan records			5 yr		13 cerebrovascular accidents: 9 with persistent deficits 1 case/1–3,000,000 manipulations
Haynes ⁵⁴	17 Australian chiropractors, 7 neurologists	Mail questionnaire	Cervical manipulation	Questionnaire	Over professional careers	All chiropractors participated; 9 neurologists were contacted, only 7 participated	2 fatal cases were reported by chiropractors; 17 cases reported by neurologist, 5 strokes/100,000 manipulations
Lee <i>et al</i> ⁴⁶	177 California neurologists	Mail questionnaire	Spinal manipulation	Questionnaire	2 yr (1990–1991)	486 neurologists were mailed, only 177 responded	101 serious adverse events: 55 strokes, 16 myelopathies, 30 radiculopathies 50% marked or severe deficits
Coulter ⁵³		The complication rate was calculated using data from a community-based study of the use of chiropractic services to provide a rough estimate of the no. cervical spine manipulations delivered in the United States, and assuming that published case reports represent 1/10 of the actual complication caseload			-	-	1.46 case serious/10,000,000 manipulations 2.68 deaths/10,000,000 manipulations
Klougart <i>et al</i> ⁴²	122 Danish chiropractors	Survey	Cervical manipulation	Questionnaire	10 yr (1978–1988)	226 chiropractors were approached, only 122 participated	5 cases of stroke; 1 resulted in death and the others in permanent neurological sequelae 1 stroke/1.3,000,000 manipulations
Lynch ⁴²	11 Irish neurologists	Postal questionnaire	Cervical manipulation	Questionnaire	5 yr	13 neurologists were approached and 11 participated	16 serious adverse events: 5 strokes; 3 TIA; 2 myelopathies; 3 radiculopathies 13 with persistent deficits

(Continued)

Table 3. Continued

Author Yr	Population	Design	Type of Intervention	Evaluation Method	Reporting Period	Nonparticipation and Missing Data	Results
Stevinson <i>et al</i> ⁴⁵	239 British neurologists	Postal questionnaire	Cervical manipulation	Questionnaire	1 yr (1 August 1998–31 July 1999)	323 neurologists were approached and 239 participated	35 serious adverse events: 7 VB strokes; 2 carotid stroke; 1 acute subdural haematoma; 3 myelopathies; 3 cervical radiculopathies; the other cases were not specified
Dupeyron and Lecocq ⁴⁷	133 French neurologists, neurosurgeons, rheumatologists and physicians	Questionnaire	Spinal manipulation	Questionnaire	2 yr (1999–2001)	240 physicians were approached and 133 participated	93 serious adverse events: 14 strokes; 64 radiculopathies; 5 myelopathies; 10 others
Reuter <i>et al</i> ⁶⁶	21 academic neurology centers within Germany	Mail questionnaire	Chiropractic therapy of the neck	Questionnaire	3 yr (?)	32 academic neurology centers were mailed and 21 agreed to participate	36 serious adverse events: 36 VB strokes

Discussion

The descriptive analysis of the data we appraised in our systematic review allowed us to conclude that complications associated with chiropractic procedures are frequent events. However, the majority of the adverse events reported are benign and transitory. This does not exclude the occurrence of serious or even life-threatening events. The heterogeneity of the study designs did not allow conducting a formal meta-analysis. Data concerning the frequency of occurrence and causal relationships were nonrobust.

Regarding our results, we conclude that adverse reactions are common after spinal manipulation, according to the only randomized controlled study published.^{35,36} Case-control studies reported an increase in the rate of stroke after chiropractic manipulation.^{37,38} Serious adverse reactions (mainly stroke) were reported in prospective studies. However, other side effects were much more common, ranging from 33% to 60.9% of patients submitted to spinal manipulation; these adverse reactions were mostly local discomfort and radiating pain. These appear frequently in the first hour after treatment and disappear within the first 24 to 48 hours (Table 2). Retrospective surveys of neurologists and chiropractors reported serious adverse reactions, namely, stroke, myelopathy, radiculopathy, and also subdural hematoma (Table 3). Other serious adverse reactions described in the case reports were: spinal fluid leak presented as intracranial hypotension,^{6,17,21,23,25} *cauda equina* syndrome,^{14,61} herniated disc,^{6,61,64} diaphragmatic palsy,⁶ and pathologic fracture of vertebra.^{15,61}

Our data are in accordance with previous studies from the literature. The first review regarding the safety of spinal manipulation was published in 1996 and identi-

fied 295 cases of complications after spinal manipulation that included 165 VBA (of which 29 were fatal), 61 cases of disc herniation or progression of radicular symptoms to *cauda equina* syndrome, and 13 other cerebral complications. There were 56 reports of other types of complications, including dislocations and fractures that were often accompanied by spinal cord compression. Disc herniation and progression to *cauda equina* syndrome occurred mostly with manipulation to the lumbar region, whereas VBA occurred after rotational cervical manipulation.⁶⁶ Another review regarding this issue described 177 cases between 1925 and 1997; the most frequently reported injuries were arterial dissection or spasm and death occurred in 18% of the cases.⁶⁰ Another systematic review, reported that about half of all patients experienced adverse events after chiropractic manipulation, which were usually mild and transient.⁶⁸

The true risk of injury due to spinal manipulation is not known; estimates of the incidence of serious adverse events from published case reports and case series are about 1 case event per 1 to 2 million treatments.^{69–71} The risk of complications has been estimated to be between 1 in 40,000 manipulations for mild complications⁵² and 1 in 400,000 to over 1,000,000 manipulations for serious complications.^{40,51,52} No serious neurologic complications were reported during 1 year among 460 physicians and approximately 150,000 cervical manipulations.⁷² These numbers are speculative because they are based on assumptions about the number of manipulations performed. Besides this, the degree of underreporting is likely to be high (in a survey 35 cases of neurologic complications were identified, none of them published before⁴⁵; Robertson cited a survey of the Stroke Council of the American Heart

Association that identified 360 unpublished cases of arterial damage⁷¹).

In the absence of accurate information from prospective studies, the best estimates on the frequency of neurologic complications after spinal manipulation are from retrospective surveys with the inherent limitation of poor recall. As observed in Table 2, the incidence of complications is quite variable, ranging from 5 strokes/100,000 manipulations to 1.46 case serious/10,000,000 manipulations, and a rate of 2.68 deaths/10,000,000 manipulations has been reported. On the basis of data from a computerized registration system in The Netherlands, a complication rate of 1 per 518,886 manipulations was reported.⁷³ Calculations based on insurance claim data suggested that among US chiropractors, there is a stroke per 2 million manipulations.⁴¹

An interesting study stated that the inclusion of a chiropractic benefit in a health plan produced a selection effect in which chiropractic patients were considerably younger and healthier than comparable medical patients.⁸ A study was conducted in Canada which objective was to understand why chiropractors and neurologists had a different perception of risk regarding spinal manipulation; the author asked whether these differences in perception could be explained in part by referral or selection bias. An analysis of data from a chiropractic malpractice insurance carrier and results of a survey of chiropractors was performed; this was compared with the likelihood that a neurologist would be made aware of vertebral artery dissection after manipulation. The difference in the number of chiropractors (approximately 3840 in 1997) and neurologists (approximately 4000 in 1997) in active practice and the fact that each patient who had a stroke after manipulation will likely be seen by only 1 chiropractor, but by 3 or more neurologists, may explain the difference in experience and the perception of risk of these 2 professions. This selection or referral bias distorts the evidence for the true incidence of these complications of spinal manipulation.⁹

Our results, through retrospective surveys (Table 3), and case reports,^{11-29,57,60,61-66} indicate the occurrence of serious adverse events. Such evidence is essentially anecdotal, and thus rarely conclusive in terms of causality. Analyzing the table presented, we can conclude that the studies where a higher number of neurologists were surveyed, were those that presented the more serious adverse reactions.^{45,46,49,54} The surveys by Coulter *et al* and Carey are more precise because they used data from legal/insurance claims, Government Health Plan records, and from a community-based study of the use of chiropractic services and published case reports, respectively.^{53,55} This data are inconclusive in terms of incidence, but the risk of occurrence of serious adverse reactions should be assumed. Chiropractic applied many different manual therapy approaches; another limitation of these studies is that they all (except 2^{34,35,38}) do not present an accurate description of the maneuver used in

the treatment protocols; they refer only to cervical/spinal manipulation.

There have been attempts to identify predictors of adverse events. Women (65% *vs.* 44% in men) and those aged 27 to 46 years (60% *vs.* 49% in 47- to 64-year-olds) were found to more likely experience side effects after spinal manipulation. Other risk factors identified were first treatment sessions, more than one region treated, or when the thoracic spine only was treated.⁷⁴ In another study, upper cervical manipulation, use of medication, and female gender were independent predictors of headache after spinal manipulation.⁴⁴

We cannot exclude the possibility that the reason why patients asked for chiropractic treatment was already creating the onset of the adverse event reported. A pragmatic approach recommends appraising these events as they happened independently of this limitation. A recent study using single photon emission computed tomography in 15 volunteers concluded that cerebellar hypoperfusion may occur after cervical spinal manipulation. This could explain why certain people experience headache, dizziness, vertigo or nausea, blurred or impaired vision,⁷⁵ and according to Vautravers, these constitute red flags that contraindicate cervical manipulation.⁷⁶ Despite the existence of screening protocols for high-risk patients, none was proven to be sensitive or specific.⁷⁷ Although, some nonvertebrobasilar complications might be avoidable by heeding contraindications for spinal manipulation,⁵⁶ VBA are more difficult to prevent because they tend to occur in relatively young, previously healthy adults.³⁶

Neither of the prospective studies included in this meta-analysis report a single case of serious, more permanent injury. This might suggest that such events are rare. One could, however, also postulate that only patients who returned for treatments were asked about adverse reactions after the previous intervention. Patients who did not return might have suffered serious complications. We also can comment on the fact that when questionnaires were answered by the patients, they present a higher frequency of side effects, meaning that the practitioners may underestimate the adverse events.^{43,44}

The remarkable popularity of spinal manipulation is contrasted by a disappointing lack of well-conducted studies to assess efficacy. Accepting that its efficacy for treatment of multiple indications is unknown, the aspects of safety gain extreme relevancy. Adverse reactions are frequent after spinal manipulation ranging from 33% to 60.9%, mostly increased pain or stiffness. However, the frequency of serious adverse events is not established varying between 5 strokes/100,000 manipulations to 1.46 serious adverse events/10,000,000 manipulations and 2.68 deaths/10,000,000 manipulations, with stroke being the most frequent. Safety in chiropractic manipulation is far from being achieved. Further investigations are urgent to assess definite conclusions regarding this issue. In the meantime, it is necessary to establish

a system of risk alert to guarantee the surveillance of this type of alternative medicine. One possible way to guarantee a safety evaluation regarding chiropractic is to include its adverse reactions in pharmacovigilance systems.

■ Key Points

- Chiropractic interventions are applied to a growing number of indications.
- Heterogeneity of study designs and safety outcomes report limits the conduction of a pooled analysis of the data.
- Complications associated with chiropractic procedures are frequent.
- Most of the adverse events reported are benign and transitory, however, some can be life-threatening.
- There is insufficient data to produce a robust conclusion on safety of chiropractic interventions.

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■ Appendix

PUBMED Search Strategy

1. Chiropractic (4043)
2. Spinal manipulation (2457)
3. One OR 2 (5581)
4. Safety (182795)
5. Adverse reactions (42090)
6. Adverse events (49462)
7. Four OR 5 OR 6 (252600)
8. Three AND 7(151)