CHIROPRACTIC RESEARCH: 2010 PRACTICE ANALYSIS

I. Introduction

A. Perspectives:

In the space of just 115 years from its inception, chiropractic has emerged as the third largest healthcare profession in the United States offering diagnostic as well as therapeutic services to patients. It has reached this lofty height driven by research which has made particularly dramatic strides over the past 30 years, supported by a budget which represents merely an infinitesimal fraction of that applied to medical and pharmaceutical research.

Like all health professions, chiropractic regularly tests the effectiveness, safety, and costs of its approaching health care. Studies continue to show that chiropractors offer the public a viable alternative to invasive healthcare (drugs, surgery) especially in the treatment of musculoskeletal problems such as back, neck, and headache pain. But chiropractic treatments are likewise effective in the treatment of non-musculoskeletal health issues, including infantile colic, enuresis, asthma, dysmenorrheal, otitis media, hypertension, and heart rate variability. And few medical professions outside of chiropractic can offer such healthcare solutions with equal safety and cost records.

Having been historically been placed in the category of "alternative and complementary" medicine, chiropractic because of its rapid growth in its research has now been deemed to have reached the crossroads of mainstream and alternative medicine.[1] As a hybrid, it appears to have successfully incorporated many of the research methodologies of orthodox medicine while striving to maintain its distinct healthcare paradigm. Indeed, when the practitioner's primary means of patient care and published randomized clinical trials supporting that intervention are matched, chiropractic can be shown to enjoy a higher percentage of interventions thus supported when compared to such other medical disciplines as general practice, inpatient general surgery, dermatology, or hematology-oncology.[2] In other words, chiropractic can now claim to have attained at least as much of a scientific grounding as other medical interventions based upon its research.

So what is it that one means by chiropractic research? The research related to the practice of chiropractic, to be reviewed in this chapter, has been presented in multiple dimensions, including:

1. Published clinical articles;
2. Literature reviews;
3. Surveys and public opinion research;
4. Analyses of insurance claims [actuarial research]; and
5. Guidelines

B. First major interdisciplinary cohort study:

One of the first lines of evidence in support of chiropractic intervention that could be considered to be more robust came in 1985 from a prospective observational study of 283 patients suffering from chronic low back and leg pain, drawn from a university back pain clinic reserved for patients who had not responded to previous conservative or operative treatment. Given a 2-3 week regimen of daily spinal manipulation by an experienced chiropractor, 81% of these patients with referred pain and 48% of those with nerve compression displayed improvements in pain grades after their assessments at 1 month followed by 3-month intervals. The research was noteworthy in that it represented a collaboration between chiropractic [David Cassidy] and medical providers [William Kirkaldy-Willis] and was published in a leading medical journal.[3]

C. Endorsements in back pain care by government agencies:

In 1979, just four years after chiropractic research received its assessment from the historic NINDS Confer-

ence, extensive investigations in 1979 by the Commission of Inquiry in New Zealand of chiropractic in the United States, Canada, United Kingdom and Australia as well as New Zealand culminated in the release of a report which concluded that modern chiropractic is a soundly-based and valuable branch of health care in a specialized area neglected by the medical profession."[4] Some thirty years later, it was evident from the extent and quality of chiropractic research that dramatic changes were in evidence. Regarding back pain as assessed by government agencies in the U.S.,[5] Canada,[6] Great Britain,[7] Sweden,[8] Denmark,[9] Australia,[10] as well as New Zealand,[11] one could argue that chiropractic care appears have vaulted from last place to first as a treatment option for musculoskeletal disorders.

For example, according to the assessment of back pain treatment by a U.S. government agency, the Agency for Health Research and Quality [formerly the Agency for Health Care Policy and Research], the strength of the evidence found to support manipulation was rated sufficiently highly to place this intervention as one of two leading options [together with the use of analgesics and nonsteroidal anti-inflammatory drugs [NSAIDs] to be considered from 27 different types of interventions reviewed.[5] The comparative gradings of evidence supporting each of these interventions are displayed in **TABLE 1**, in which spinal manipulation was only one of two options found to have a positive effect with as high as a "B" grade. The British guidelines lauded that "there is considerable evidence that manipulation can provide short-term symptomatic benefits" in certain patients,[7] while the Danish report echoed this sentiment by declaring that "manual treatment can be recommended for patients suffering from acute low-back symptoms and functional limitations of more than 2-3 days duration."[9]

II. The State of Evidence-Based Practice

A. Definitions of EBM:

"Evidence-based medicine" [EBM] was introduced as a term to denote the application of treatment that has been proven and tested "in a rigorous manner to the point of its becoming 'state of the art.'"[12] Its intention has been to ensure that the information upon which doctors and patients make their choices is of the highest possible standard.[13] To reach a clinical decision based upon the soundest scientific principles, EBM proposes five steps for the clinician to follow as shown in **TABLE 2**.[14] **Step 2** [accessing the best evidence] customarily follows a totemic relationship of the available designs of clinical research, shaped as a pyramid and shown in **FIGURE 1**.[15]

Here it is evident that systematic reviews and meta-analyses occupy the rarefied top echelon, followed by randomized controlled double blind studies [RCTs] and thence by cohort studies, case control studies, case series, and case reports. It is only at the second rung from the bottom that one discloses what is presumed to be the lowly category of "animal research." This is clearly an absurd finding, the ramifications of which will be discussed below in **Section IIIA.**

It is also apparent in **Step 4** of **TABLE 2** that there has been a "greening" of the original concepts of simply rating evidence by the paint-by-the-numbers approach of simply grading the evidence of published research papers. For here the epidemiologist David Sackett has made clear that such realities as patient subgroups and comorbidities play a major role in therapeutic decisions, such that **clinical judgment** becomes recognized as significant as well:[16]

"[EBM] means integrating individual clinical expertise with the best available external clinical evidence from systematic research. By individual clinical expertise we mean the proficiency and judgment that we individual clinicians acquire through clinical experience and clinical practice. By best available external clinical evidence we mean clinically relevant research, often from the basic sciences of medicine, but especially from patient centered clinical research into the accuracy and precision of diagnostic tests [including clinical examination], the power of prognostic markers, and the efficacy and safety of

therapeutic, rehabilitative, and preventive regimens. Good doctors use both individual clinical expertise and the best available external evidence, and <u>neither alone is enough</u> [emphasis added].
Without clinical expertise, practice risks becoming tyrannized by external evidence, for even excellent external evidence may be inapplicable to or inappropriate for an individual patient. Without current best external evidence, practice risks becoming rapidly out of date, to the detriment of patients."

<u>B. Limitations of EBM and Transformation to "Evidence-Informed" Best Practices</u>:

Cracks in the foundation of one of the strongest pillars of conventional definitions of EBM based upon the pyramid shown in **FIGURE 1** began to appear in the 1980s, when the quality of observational [cohort, case series] studies was found to improve, such that their

predictive value in clinical situations could now be compared to that seen in the more rigorous RCTs.[17,18] At the same time, RCTs began to be seriously challenged due to their limited applicability in clinical situations.[19,20] Among other problems, RCTs were found to lack insight into lifestyles, nutritional interventions, and long-latency deficiency diseases.[21] Quirks have likewise surfaced which demonstrate how even the exalted meta-analysis is subject to human error and bias.[22]

In addition to factoring in the judgment of the clinician to EBM, effective patient care requires, in the final analysis, the **attributes of the actual patient**. Such patient-based outcome measures as the **Health Related Quality of Life Index** and **cost-effectiveness** will continue to grow as elements which cannot be ignored in EBM. Indeed, it has been argued that "the most compelling and growing" component of EBM is the empowerment of the patient in the decision-making process.[23] With patients being the best judge of values, clinical decisions are becoming recognized as necessarily shared between the patient and clinician.[24]

This shifting of the EBM sands echoes what a few years ago appeared to be a revolutionary upheaval suggested by Wayne Jonas, who presented what appeared to be for all intents and purposes a virtual inversion of the classical evidence pyramid. In Jonas' presentation of the "evidence house," such entities as use testing, public health, and audience preferences gained ascendancy.[25]

Despite all these revisions, these upgrades of EBM have not been able to outrun all of the most severe critics of EBM. When EBM is applied in a unilateral, heavy-handed manner, it has run the risk of becoming a "regime of truth" in such a manner as to discourage free inquiry. Put in other terms, it is questionable whether many current models of EBM promote the multiple ways of knowing considered to be important in most health disciplines,[26] falling under a spell which Foucault has referred to as a "clinical gaze."[27] For these reasons, proponents of EBM have fallen back to a position in which the best evidence is now considered to **guide** or **inform** rather than mandating a clinical decision.[28,29]

III. Basic Research

A. Importance of Test Organisms:

The two key reasons for seeking a test organism in research are that: [i] it presents a simplified picture of an area of interest, maintaining its essential features; and [ii] it lends itself to experimental manipulations which are more difficult or impossible in the more complex [usually human] arena. One prominent feature and advantage of the test organism is that it allows direct examination of living tissues, shedding further light upon complex biological interactions. According to Howard Vernon, animal models as a class of test organisms enable the investigator to:[30]

1. Test theories derived from conceptual models.
2. Provide data to support clinical experience.

3. Apply a high degree of experimental control.
4. Explore cause and effect relationships from prospective studies.
-5- Explore "treatment" effects when a lesion is reversed.
6. Explore physiologic components of subluxations.
7. Explore behavioral effects in chronic experiments.

Medicine could not have developed without the use of test organisms. This would encompass everything from our understanding of genetic principles from the plants of Gregor Mendel or the bacteria on the Petri dishes of Alexander Fleming, Seymour Benzer, or Bruce Ames. It extends to the treatment of anthrax from the sheep of Louis Pasteur, the isolation of insulin by Banting and Best from dogs, and the identification of the conditioned reflex from Ivan Pavlov's dogs. Indeed, no less an authority than the British Royal Society of Medicine argues that virtually every major medical advancement of the 20th century relied upon the use of animals in some fashion.[31]

Chiropractic research is no exception. As Charles Henderson has so aptly pointed out, even the *differences* between animals and humans have opened the way to major discoveries essential for understanding basic concepts in neuroscience.[32] Thus giant squid axons that are 100-1000 times larger than their mammalian counterparts have given researchers the opportunity to measure the ionic composition of neural cytoplasm and study changes in membrane potentials.[33] The eggs of the clawed African frog, Xenopus laevis, have allowed the development of patch clamp technique to study ionic currents generated by newly formed channels.[34] More recently, degenerative changes following spinal fixation that could be considered attributes of the subluxation have been identified in the rat.[35] This followed the groundbreaking experiments in the 1980s by Sato and Swenson who clearly identified changes in the sympathetic nervous system that followed mechanical stresses to the spinal column in rats.[36] And finally there has been a proliferation of data from Xue-Jun Song which have demonstrated the multifaceted analgesic effects of instrument-assisted manipulation[37] or the administration of the B-vitamins[38] in rats which have been subjected to neural injury. These are but a very few examples of the significant advances in our understanding of the physiological processes which attend human disorders and their alleviation through healthcare management.

B. Anatomy:

A key concept of chiropractic has consistently been the relationship between structure and function. That said, numerous investigations into the associations of spinal structures and neurons shed considerable light upon the possible mechanisms of the manipulative techniques of the spine specified in chiropractic healthcare, as well as the disorders that they were designed to treat.

Clinically significant relationships between spinal structures and neural elements could be deduced from the earlier surface cryoplaning technique described by Rauschning, whose observations of degenerative changes of the intervertebral foramina [IVF] revealed encroachments of the nerve root complex and radicular vessels upon extension and

rotation of the specimen.[39] Transforaminal ligaments, shown to cause a significant decrease of IVF size,[40] were later identified as possible agents of nerve root entrapment. In the upper spine, overlapping connections between neurons in the neck and head and face provided a mechanism for the referral of upper cervical dysfunction to the head, offering a rationale for the chiropractic treatment of some cases of headache.[41]

Measuring the endoneural fluid pressure in the dorsal root ganglia of rats, Rydevik provided an explanation as to how pressure on the DRG could lead to radicular symptoms.[42] As far as linkages to back pain were
concerned, a number of investigations by Bogduk and Groen described the innervation of the intervertebral disc [IVD in the lumbar region[43,44] and the anterior and posterior longitudinal ligaments.[45]

A major pillar of chiropractic theory suggests that an essential component of the vertebral subluxation complex is the development of adhesions in the zygopophysial joints as the result of hypomobility which develops in these structures,[46,47] and that spinal manipulation would be capable of breaking up these fixations in a process known as "gapping."[48,49] The finding by Cramer and his colleagues that gapping did indeed occur in healthy volunteers subjected to spinal manipulation[50,51] therefore provided noteworthy

support to this aspect of chiropractic theory.

Another productive line of inquiry regarding anatomical components of the spine involves connective tissue attachments to the spinal dura mater. The posterior aspect of the spinal dura appears to be anchored by bridges from the foramen magnum, posterior arch of C1, spinous process of C2,[52] the rectus capitus posterior minor muscle,[53] the ligamentum nuchae,[54] and the ligamenta flava between C1-C2 and C6-C7.[55] All these attachments are proposed to retain the dura mater posteriorly during cervical extension [to prevent buckling of the dura mater into the spinal cord] and flexion [to prevent forward movement of the dura which would compress the spinal cord]. Their role would prevent dural tension leading to headaches[56] or other forms of neck pain and cervical myopathy.[54]

An additional area of recent anatomical investigation has involved scoliosis, whose cause remains unknown and which has been highly refractory to treatment. A group of rats developed thoracolumbar scoliosis within a week after dental derangement [an induced malocclusion] such that the resulting tilt of the C1 vertebra could affect the alignment of the adjacent vertebrae and lead to the destabilization of the vertical alignment of the spine.[57]

One model which appears to reconcile a broad range of patient presentations with the characteristics of the spinal subluxation is **buckling**, defined as a deformation within the multisegmented nature of the spinal column caused by an overload and/or muscle stiffness which falls short of its intended activity. Buckling then leads to a concentration of local tissue stress which, if sufficiently large, will lead to pain and inflammation.[58,59]

A final element of considerable importance to the safety of manipulation is the vertebral artery, a topic to be discussed in further detail below [**Section V**]. The composition of the vertebral wall has been discussed in some detail by Rosner, essential for understanding how arterial integrity may be compromised by natural causes.[60] Numerous recent studies have indicated that blood flow following extreme rotation and extension appears to decrease.[56,61,62]

C. Biomechanics:

At the core of biomechanics research is the assessment of the interaction of imposed mechanical forces and the bones, muscles, ligaments, and other soft tissues which experience them. This understanding is essential for chiropractors, whose primary objective is to restore balance and mobility to the spinal column and other musculoskeletal structures subjected to translational, rotational, compressive and distractive forces.

John Mennell did much to emphasize the heart of biomechanics, stressing that the loss of a functional movement demanded a return to mechanics. Loss or alteration of movement was understood to accompany the pain treated by a chiropractor, the element of interest being **joint play**.[63] This required a thorough understanding of the forces internally at the joint surfaces, in addition to those experienced when the practitiioner's hand meets the patient's body.

These principles were advanced in numerous investigations, harking back to the studies of Janse and Illi in the 1940s.[64,65] More recently, Adams and Wood were able to determine peak normal forces, their duration and impulses by inserting a force transducer between the hands of practitioner and a model of the patient's body.[66] These results were subsequently refined in the 1990s by Herzog, Kawchuk, Conway and others at the University of Calgary, applying these measurements to different techniques of manipulation to all regions of the spine.[67,68] Carrying this line of inquiry forward, Triano and Shultz[69] demonstrated in a study involving 6 chiropractors employing 3 different techniques [each on 11 patients] that:

1. Precise forces of manipulation at the joint surface are significantly influenced by the type of technique as well as patient posture;
2. Clinically significant forces are delivered at the joint surface level; and
3. These forces approximate those seen in common daily tasks, such as on jobs requiring lifting and twisting movements.

More specific force measurements at the vertebral areas affected by adjustments was accomplished either by surgery or using intact cadaveric human spine specimens. In patients undergoing lumbar surgery, Keller found peak displacements of the vertebrae of about 0.6 mm within 10 milliseconds at forces of 30N-150N, as applied either by

mechanical force with the Activator as an adjusting instrument or by very high-velocity thrusts.[70] In cadaveric human lumbar spines, vertebral translations were 1-2 mm, rotations were 1-3^{o}, and capsule strain magnitudes were approximately 5% after simulated high velocity spinal manipulations.[71]

Turning to the use of geometric data, a number of investigators performed displacement measurements in live subjects. One such approach was to assess in vivo spine motion by digital video fluoroscopy.[71] Another was to assess the motion of the patient's head during two different techniques of cervical manipulation.[72] A third was to measure the effect of loading frequency on spine stiffness and nonlocal displacement effects in the lumbar region by employing machine-controlled cyclic mobilizations.[73] Combining both force and geometric measurements, Van described the 3-dimensional force applied during high-velocity, low amplitude manipulations of all regions of the spine.[74]

Arguably one of the most inclusive models of subluxation and the application of biomechanics has come from the novel external fixation model in rats described by Cramer, Henderson and coworkers at both the National University of Health Sciences and Palmer University. Here the spinous processes of L4-L6 were fixed by a noninvasive, removable yoke for up to 8 weeks [**FIGURE 2**]. Osteophytes and degenerative articular changes of the facet joints could be observed for fixation times as short as 1 week and became irreversible after 4 weeks of fixation.[35] Changes in spinal stiffness were also noted, being greater in magnitude and producing greater misalignments during forced extension testing for longer linked periods before removal of the yoke.[75]

D. Neurology:

Harking back to Solon Langworthy's assertion that the core of chiropractic principles lies in the nervous system],[76] we need to review some of the key research accomplishments relating to neural activity in response to both manipulations and the dysfunctions they are intended to treat. For it is indeed the nervous system which provides the necessary communication links to hormonal, inflammatory, immune and visceral activity in addition to pain perception--all of which are to be discussed later in this chapter.

A wide variety of neurophysiologic studies are simply not possible to perform in humans; thus, animal models once again come to the forefront for providing the necessary evidence for chiropractic in the basic sciences. **TABLE 3** is a sampling of some of the earlier outcome effects achieved in a variety of animals as the result of different types of interventions, all involving noxious stimuli. [36,77-86] Quite distinct from pain are effects which extend far from the area of stimulation. With several of the investigations showing that nerve conductivity is specifically affected,[77,78,83] it is clear that the **nervous system** provides an essential link between the experimentally produced aberrations and the physiological changes observed. Additional investigations using rats have been able to elicit decreases in both mean arterial pressure and nerve blood flow following saline injections into the ipsilateral L4/L5 facet joint.[87] Further experiments by the same investigator [Sato] demonstrate decreased gastric motility in response to a somatic

stimulation [skin pinch].[88]

Thus, a wide range of stimuli are capable of producing physiological responses, providing a much broader canvas with which subluxations can be represented in experimental research and again placing the nervous

system at the center.

The complete description of the autonomic nervous system and its division into the sympathetic and parasympathetic branches is beyond the scope of this chapter, but is provided elsewhere.[89] With regards to *changes in neural function in response to either stress or manipulation*, however, several observations can be brought to light:

1. Insertion of a small pin into the IVF of the L4 and L5 vertebral joints of the experimental rat, mimicking a space-reducing lesion, produces thermal and mechanical hyperalgesia in the hind limb and increases the excitability of dorsal root ganglion cells.[90,91] The same responses are observed with the injection of an inflammatory cocktail into the same region.[37]

2. Reflex responses in para spinal muscles are attenuated by activating Z-joint receptors in rats, regarding noxious stimulation of nerves in the intervertebral disk. Accordingly, there may be interaction between spinal joint receptors and the processing mechanisms for spinal reflexes.[92]

3. Abnormal somatosensory evoked potentials from the paraspinal musculature are found correlating with decreased pain responses after lumbar manipulation, possibly due to a central effect of sensory processing.[93]

4. In a cohort of 12 subjects with a history of recurrent neck stiffness and/or neck pain but no acute symptoms at the time of study, a single session of cervical spine manipulation reveals a significant decrease in the amplitude of 2 components of somatosensory evoked potentials, lasting 20 minutes following the intervention. The implication is that cervical spine manipulation may alter cortical somatosensory processing and sensorimotor integration, shedding light upon the mechanisms for the relief of pain and restoration of functional ability which are the most widely observed outcomes to treatment by spinal manipulation.[94]

5. In subjects subjected to side-posture manipulation, both Hoffman reflex and M-wave responses display the greatest attenuation with actual manipulation--as opposed to a positioning maneuver.[95]

6. Following SI joint manipulation, there is a decreased inhibitory effect of knee joint pathology on quadriceps muscle activity, suggesting an interaction between spinal manipulation and the inhibition of voluntary activities produced by pain.[96]

7. Power spectrum analyses of patient electrocardiograms suggest alterations of sympathetic and parasympathetic activity produced by spinal manipulation.[97-99]

8. In the experimental cat, muscle spindles and Golgi tendon organs in para-spinal muscles respond to vertebral loads with force-time profiles resembling those in spinal manipulation.[100] The proprio-receptors, displaying a unique response to the thrusting portion of the applied load suggests that these receptors might contribute to the therapeutic effects of spinal manipulation.[101]

E. Hormones:

The manner in which the endocrine system relates to chiropractic is best represented through three approaches:

1. The way pain is associated with the endocrine system and the implications in the relief of pain through spinal manipulation;
2. The way stress is associated with the endocrine system and the way its detrimental effects on health may be relieved by spinal manipulation; and

3. A description of specific endocrine disorders and their responses to spinal manipulation.

The psychologic and psychosocial influences on the course of human disease have led to the science of psychoneuroiimunology [PNI] used to describe the communication system between the mind and body.[102,103] A considerable body of research established that through a complex system of feedback loops and interactions, a close communication among the CNS, the immune system, and hormones by means of the hypothalamic-pituitary-adrenal [HPA] axis existed[104] [**FIGURE 3**].

Once stress is experienced, distinct chemical entities including the neuropeptides and neurohormones function as a primary means of intercellular communication. The end result is the complex pathway shown in **FIGURE 4**, the most important aspect of which is the secretion of corticosteroids--in particular, glucocorticoids [including cortisol] from the adrenal cortex in response to adrenocorticoid [ACTH] secretion from the anterior lobe of the pituitary. Glucocorticoids subsequently exert a variety of effects on the cardiovascular system, muscle, and immunologic activity--much of which is detrimental. Connections between increased cortisol levels and stressful events has been well documented.[105,106]

The fact is that chronic stress has been shown to promote an extensive variety of disorders, some of which are life threatening. These include: [a] infections from cold viruses[107] and herpes;[108] heart disease;[109,110] gastrointestinal dysfunction;[111] insulin-dependent diabetes mellitus [in animal models];[104] and systemic lupus erythematosus.[103]

The most direct evidence that chiropractic appears to relieve **stress** is from two recent randomized clinical trials. One found that spinal manipulation significantly reduced the intensity of emotional arousal reported by phobic college students.[112] A second demonstrated significant reductions in validated anxiety, depression and stress scores in asthmatic patients who were manipulated, as opposed to those who merely reported to chiropractic centers for consultation.[113] The previous trial and two additional investigations involving either chiropractic manipulation[114] or massage[115] indicated the spinal manipulation may also reduce salivary cortisol levels.

The evidence that chiropractic is effective in relieving **pain**, reviewed below in **Section IV**, is mentioned here in its possibly being mediated by two hormonal metabolites found to respond to spinal manipulation. Beta-endorphins [enkephalins] have been proposed to display a gating, palliative effect at the first synaptic relay in the spinal cord, limiting the transmission of pain information from the peripheral pain receptor to the brain.[116] Investigations by Vernon[117] revealed approximately an 8% increase in the level of plasma endorphins 5 minutes after a single rotary manipulation in asymptomatic men. This effect was not repeated in other studies;[118,119]; however, only Vernon's study employed measurements timed to more closely match the rapid postintervention physiologic events suggested by others[120] and are more indicative of the short half-life of plasma beta-endorphin.[121] Two specific forms of the prostaglandins, the hormones responsible for uterine contraction and suspected to be the cause of menstrual pain in dysmenorrhea, were found in a pilot study by Brennan to be suppressed together with menstrual pain after side-posture manipulation, as opposed to patients who received a low-force sham procedure.[122] Inconclusive results were obtained in a follow-up full-scale randomized clinical trial;[123] however, major design flaws in that particular investigation have virtually invalidated its results.[22]

In addition to the hormonally driven dysmenorrhea being relieved by spinal manipulation,[122, 124-127] numerous endocrine disorders have been reported to respond to spinal manipulation. These include premenstrual syndrome,[128-130] hypertension,[131-134] and even extremely preliminary single case reports suggesting that diabetes[135] and hot flashes during menopause[136] could diminish as well. One additional trial failed to distinguish a difference in the blood pressures of dieting patients, with or without spinal manipulation included
In treatment.[137] To explain this particular discrepancy, both the chiropractic technique and frequency of manipulation need to be explored further.

A comprehensive description of the endocrine system and its relation to chiropractic has been provided elsewhere.[138]

F. Inflammation:

Inflammation is a twofold response of the vascular tissue in an organism, both to remove harmful stimuli--such as pathogens, damaged cells, or irritants--or to initiate healing. In

the acute phase, it can be experienced by redness, pain, heat, swelling, and loss of function. The immune system and a variety of cells within the injured tissue participate as well. At the site of cellular injury, the locus of pain in the peripheral nervous system, a cascade of chemical events occurs. It is characterized by the production of arachidonic acid and its conversion by cyclooxygenase to intermediates ultimately resulting in the production of the prostaglandins. This sequence is depicted in **FIGURE 5**.[139]

If left unchecked, this process becomes chronic and can lead to a number of conditions including hay fever and other allergies, inflammatory bowel diseases, rheumatoid arthritis, autoimmune diseases, and atherosclerosis. Playing a central role in several stages of atherosclerosis are the **cytokines**, which are neuropeptides acting like hormone messengers to integrate the functional activity of other immune cells.[140] They orchestrate the production of adhesion molecules, matrix metalloproteinases, and reactive oxygen species that may also be released from lesions. Particularly active in this capacity is the pro-inflammatory cytokine interleukin IL-6, which travels to the liver and elicits an acute-phase response, resulting in the release of C-reactive protein, fibrinogen, and plasminogen activator inhibitor [PAI]-1, all essential components to the development of atherosclerosis.[141,142]

It turns out that control of this process can be linked directly to chiropractic, in that preliminary evidence in both animal models and humans suggests that spinal manipulation may be effective in retarding or reducing several indicators of inflammation.

By injecting an inflammatory cocktail directly into the L5 intervertebral foramen of experimental rats, Song and his colleagues were able to evoke a broad spectrum of indicators of neural excitability and inflammation, including [i] thermal hyperalgesia, demonstrated by quicker foot withdrawal in response to heat; [ii] mechanical allodynia, shown by more rapid foot withdrawal in response to touch; [iii] hyperexcitability of the dorsal root ganglia, revealed by electrophysiological recordings; and [iv] vascularization and satellitosis, seen as cellular inflammations under the microscope. All these indicators diminished with time following the application of mechanical manipulations to the L5 or L5 and L6 spinous process by means of the Activator adjusting instrument; no such effects if the manipulation was directed to the L4 joint. The implication was that mechanically applied manipulation can significantly reduce the severity and duration of pain and hyperalgesia caused by inflammation of the lumbar intervertebral foramen.[37]

This narrative shifts to humans with the finding by Teodorczyk-Injeyan that asymptomatic humans who are subjected to a bilateral hypothenar thrust procedure in spinal manipulation and who experience a cavitation display a marked decrease in their blood serum levels of the pro-inflammatory cytokines.[143] At the same time, levels of the anti-inflammatory cytokines *increased*.[144] Neither effect was observed in the absence of cavitations.[143,144] To close this intriguing circle of evidence linking spinal manipulation and the control of the potentially lethal pro-inflammatory cytokines, further research is necessary to determine whether these effects can be duplicated in: [i] humans experiencing back or other types of pain, and [ii] experimental rats. One vital step in this direction is a recent finding that the pro-inflammatory cytokines IL-1 alpha, IL-1 beta,

tumor necrosis factor alpha, and IL-6 are all elevated within weeks in experimental rats which are subjected to repetitive motion injuries.[145] Thus we are left with the intriguing possibility that spinal manipulation may be able to retard or forestall potentially life-threatening human conditions.

IV. Outcomes Research

A. Methods of Measurement:

1. Design issues:

As in other outcomes clinical research, chiropractic investigations require reproducible and verifiable measurements from multiple points of view involving both the patient and clinician. **TABLE 4** illustrates five such perspectives: [1] the results of physical examinations; [2] functional abilities; [3] patient perception regarding pain, satisfaction, duration of complaint, and use of medications; [4] general health and psychosocial assessments; and [5] direct and indirect costs of treatment. All these indices have been verified in the literature; use of the measures represented on this list helps to ensure that an outcomes study achieves sufficient construct validity.

At the same time, outcomes research [particularly involving physical interventions] is tarnished by what appears at first glance to be a conundrum. **FIGURE 1** has listed outcome studies in order of decreasing rigor, from the most fastidious, demanding [and costly] RCT to anecdotes arising from everyday clinical experiences. One might assume at first that the most controlled investigation [the clinical trial] would yield the most useful information. Indeed, the clinical trial has been referred to as the **"gold standard"**[146] in clinical research. But paradoxically, because the double-blind study is so controlled, this most rigorous member of the clinical research hierarchy presents its own difficulties in its generalizability:

1. The characteristics of its own experimental patient base [including comorbidities] may differ significantly from those of the individual presenting complaints in the doctor's office.
2. Potentially important ancillary treatments are restricted, screening out conceivably significant and perhaps unidentified elements that occur in the natural setting of the patient's visit to the physician.
3. Outcome results chosen may not necessarily be those used to evaluate a patient's welfare under care of an actual physician.
4. Experimental groups may not be large enough to reach statistical significance, even though the clinical effect may be real in many individuals.

Thus, experimental designs at the "lowly" end of the spectrum, such as anecdotes, single case reports, offer their own form of generalizability, although they are of an uncontrolled and often confounded nature. Again, this does not mean that they fail to provide clinical

significance. Ideally, to support a particular type of intervention, what is needed are research results from both ends of the hierarchy shown in **FIGURE 1**, to capture both the rigor and the generalizability sought in clinical documentation. It is, after all, material from the anecdotes and clinician's office that provide the impetus and inspiration to design and conduct an RCT in the first place.

2. Systematic reviews, meta-analyses:

In an effort to filter out low-quality studies, rating systems of trial quality have abounded as an attempt to assure that that the edifice of evidence used to warrant a therapeutic approach is more than a house of cards. These form the cornerstone to both systematic literature reviews and meta-analyses, the former defined as a comprehensive and rigorous review of the peer-reviewed scientific literature requiring a predetermined threshold of graded quality in order to be included. In *meta-analyses*, on the other hand, actual effect sizes are calculated from pooled results of different clinical trials using a variety of statistical procedures and taking into account the size of each study.

A multiplicity of scoring systems for trial quality exists, but their essence is perhaps best reflected by the rating chart shown in **TABLE 5**. It is taken from a recent blend of narrative and systematic reviews by a group of leading clinical chiropractic researchers headed by Gert Bronfort.[147] What is perplexing is that two out of

the eight criteria for quality recognize **blinding of the patient or practitioner** as an attribute for quality ratings. As mentioned previously, successful blinding of these parties in any trial involving physical interventions is virtually impossible.

This is only the beginning of limitations of systematic reviews and particularly meta-analyses. In a critique of the latter design, Feinstein argues that some of their problems include:[148]

1. Disparate groups of patients of varying homogeneity across different studies are tossed into one analysis like a mixed salad, overwriting the clinician's need to know about subgroups which relate more to the patients actually seen.
2. The weighting of studies of different quality may be inaccurate or absent altogether.
3. There is the need to know about real-world effects [severity in illness, comorbidities, changes in schedule, pertinent co-therapies, and clinically relevant outcomes] in presentation and treatment.
4. The statistical treatments in the papers pooled are inconsistent.

As a means to alleviate the limitations of randomized clinical trials, systematic reviews, and meta-analyses, modified designs based upon a blending of observational and experimental studies have been proposed. Among these are **Pragmatic Clinical Trials [PCTs]** and **Whole Systems Research [WSR]**.

PCTs ask practical questions about the risks, benefits, and costs of intervention as they

would occur in routine clinical practice. In addition, they include a diverse population of study participants, recruiting from a variety of practice settings and collect data from a broad range of health outcomes. The interventions which they select are clinically relevant.[148]

WSR uses observational studies and includes qualitative as well as quantitative research. In so doing, it provides the opportunity to assess the meaning that patients attribute to an intervention, probing the process and context by which healing occurs. Outcomes which are relevant to the patients are selected, and the approach explores how the intervention fits with a patient's life.[150] In so doing, it reveals the role that **expectations** may play in healing.[150] Essentially, WSR seeks to describe the effectiveness of the entire clinical encounter rather than simply a single procedure.[151]

B. Musculoskeletal:

1. Back pain research:

a. The RAND Appropriateness and Utilization Study:

An early milestone in musculoskeletal disorders research with regard to the back and chiropractic can be credited to the RAND Corporation, a non-profit private corporation which conducts research and development [hence, the acronym] and which gained prominence with research for the U.S. military during World War II. In addition to defense, RAND's research fields include the health sciences, education, applied economics, sociology, and civil justice.

Several years and millions of dollars in the making, the RAND Appropriateness and Utilization Study sought to to provide "a comprehensive set of indications for performing spinal manipulation with low back pain," the guidelines being based upon [1] a review of the literature, [2] appropriateness ratings by both multidisciplinary and all-chiropractic panels of experts and [3] field studies abstracted from five geographical sites: Portland, OR; Minneapolis, MN; Miami, FL; San Diego, CA; and Toronto, ONT.

The significance of the literature review of 67 articles and 9 books published between 1952 and 1991 lay in the fact that it established that chiropractors within the United States performed 94% of all the manipulative care for which reimbursement was sought, with osteopaths delivering 4% and general practitioners and orthopedic surgeons accounting for the remainder.[152]

Support was consistent with the use of spinal manipulation as a treatment for patient with acute low-back pain and an absence of other signs or symptoms of lower limb nerve-root involvement. If minor lower limb neurological findings or sciatica was present, the evidence was then deemed to be either insufficient or conflicting. There was no systematic report on the frequency of complications.

The appropriateness of chiropractic spinal manipulation was assessed by two expert panels, one multidisciplinary and one all-chiropractic, each rating a comprehensive array of over 1500 clinical scenarios for appropriateness or inappropriateness of chiropractic intervention. These scenarios were characterized by length of symptoms, clinical course of the pain, presence of comorbid diseases, history in response to previous treatments for back pain, findings upon physical examination, and findings on lumbosacral radiographs as well as CT or MRI. Among the appropriate conditions recognized by the **multidisciplinary** panel[153] for chiropractic intervention were [1] acute [<3 weeks' duration] back pain with the absence of neurological findings, or [2] acute back pain with minor neurological findings and uncomplicated lumbosacral radiographs. In the final ratings, panelists rated 7% of all conditions as appropriate--although these conditions represent the majority of back pain patients. As might be anticipated, the **all-chiropractic** panel[154] rated a higher percentage [27%] of all conditions as appropriate. Inappropriate ratings by the multidisciplinary and all-chiropractic panels were 60% and 48%, respectively. Amongst the all-chiropractic panel as opposed to the multidisciplinary panel, there was greater agreement [63% vs. 36%].

Depending upon the criteria for assessment, the field studies have yielded varying levels of appropriateness of chiropractic intervention. These have been grafted onto the recommendations of each of the two expert panels described above. For one site [San Diego, CA], the level of appropriateness varied between 38% and 74% and the level of inappropriateness ranged from 19% and 7%, depending upon whether the criteria of the multi-disicplinary or the all-chiropractic panel were applied. Data from other geographic areas of the United States will be required before inferences for the national population can be drawn, although it has been demonstrated that such a study is feasible.[155] These investigations simply served as forerunners for many different types of studies, all of which provided substantial evidence in support of the chiropractic management of back pain.

b. More recent achievements:

1] Systematic reviews and guidelines:

Interestingly, the earlier guidelines and systematic reviews of randomized clinical trials addressed to back pain and manipulation emphasized acute rather than chronic low back pain as having the more robust evidence in support of manipulation's effectiveness.[5,156,157] By 1997, however, more evidence supporting the effectiveness of spinal manipulation compared to other interventions became more apparent for **chronic** as well as for acute conditions.[158] That trend has held up through the more contemporary systematic reviews of Bronfort[159,160] and very recently by the Scientific Commission of the Council on Chiropractic Guidelines and Practice Parameters [CCGPP].[161] Bronfort's systematic review indicates that with all patients with chronic low-back pain, there is moderate evidence that [i] spinal manipulation with mobilization is superior to usual medical care for patient improvement; and [ii] high-dose manipulation is superior to low-dose manipulation for pain reduction in the short term. In randomized clinical trials in which most, but not all, patients had chronic low-back pain, there is moderate-to-strong

evidence that: [i] manipulation is superior to usual medical care alone; and [ii] manipulation with mobilization is superior to physical therapy and to home exercise in the long term.[160]

The CCGPP literature synthesis represented a blending of [i] a consensus process developed at RAND,[162] [ii] the Cochrane Collaboration review of literature for low-back pain, [iii] the guidelines developed by what had been the Agency for Health Care Policy and Research,[5] and [iv] published recommendations for the development of clinical guidelines.[163] In retrieving 64 randomized clinical trials, 12 guidelines, 13 systematic reviews and meta-analyses,

and 11 cohort studies, the Commission reviewed the evidence in support of spinal manipulation as a means to reduce symptoms and improve function in low-back pain patients and concluded that "as much or more" evidence exists for managing chronic as for acute and subacute conditions. For the cross-section of treatment approaches taken, the Commission issued ratings of the strength of evidence in their support as shown in **TABLE 6**.[161]

In the interim from 1992-2008, however, several systematic reviews came to less sanguine conclusions. Assendelft concluded in 2005, for instance, that there is no evidence that spinal manipulation therapy is superior to either standard treatments for patients with acute or chronic low back pain.[164] To begin, this could be interpreted in the same breath to indicate that, in terms of the pain or disability outcomes scales evaluated, spinal manipulation is not inferior. A second systematic review suggested that spinal manipulation "has small clinical benefits that are equivalent to other commonly used therapies" and does not reduce the costs of care following an initial course of therapy.[165] And a third which called itself a systematic review of systematic reviews concluded that the data fail to demonstrate that spinal manipulation is effective for a wide variety of medical problems. For back pain, spinal manipulation was deemed to be superior to sham manipulation but not conventional interventions--and the prevalence of adverse events discouraged its use.[166] All of these reviews, however, are fraught with significant weaknesses such that they must be interpreted with extreme caution, if not skepticism. These flaws are summarized in **TABLE 7**.

In terms of resolving conflicting reviews, the devil clearly is in the details. For example, in a recent presentation at a chiropractic research conference sponsored by the Health Resources and Services Administration,[167] Gert Bronfort emphasized how apparently related reviews actually embodied differing goals and methodologies, such that they could easily be misinterpreted or confused. With regard to back pain, for instance, the contrast between the Assendelft[164] and Bronfort[159] reviews can be demonstrated as follows:

Assendelft[164]	Bronfort[159]
To assess if SMT is better than anything else, to assess	if SMT is an effective treatment.

Stastical pooling using an unusual method Statistical pooling is not possible,
SMT is only equal to sham therapy or therapy judged SMT offers more short-term relief than to be ineffective or even harmful mobilization or detuned diathermy

2] Practice-based research for chronic low back pain:

An early and most dramatic example of a Pragmatic Clinical Trial [See **Section IV.A.2**.] as part of the strategy to employ **practice-based research** was provided in 1990 by Meade. A total of 741 patients at 11 clinical centers were randomized to receive either chiropractic or conventional hospital treatment in their respective natural settings. In contrast to many trials in which the relief of an intervention is observed for only a brief period, the Meade study followed patients for two[168] and three[169] years and showed that patients undergoing chiropractic treatment yielded disability scores that were lower than those experienced by the conventionally treated cohort by a clinically significant amount. One problem that has been raised regarding the Meade study, however, is that only 28% of its patients were randomized into the chiropractic branch of treatment.[169]

These findings were buttressed and expanded in a later study involving 2870 patients with acute and chronic low back pain who visited either medical or chiropractic physicians' offices and given customary care. By 2 weeks, maximizing at 1 month, and persisting for 2 years, clinically important advantages in both pain and disability scores were found in patients experiencing chiropractic treatment. A real-world outcome typical of practice-based research was shown by the number of pain days within the past year recalled by patients, substantially fewer being reported by the chiropractic cohort [**FIGURE 6**].[170]

3] Comparisons with acupuncture, NSAIDs, muscle relaxants:

One of the most dramatic outcomes in a randomized clinical trial was offered by Giles and Muller in a multidisciplinary spinal pain unit of the Townsville General Hospital in Australia. Here, 115 patients experiencing chronic [>13 weeks] of back and neck pain were randomly allocated to either medication with NSAIDs [Celebrex or Vioxx], needle acupuncture, or chiropractic spinal manipulation by means of high-amplitude, low-velocity applications to a vertebral joint. At the end of 9 weeks of treatment, the highest proportion of individuals reaching full recovery [asymptomatic status] was found for manipulation [27.3%], followed by acupunture [9%] and medication [5%]. For improvements in disability [Oswestry scale], and range of motion, the chiropractic cohort again displayed superior outcomes. While improvements in pain scores [VAS] for the back were greatest for the chiropractic intervention [50% vs 15% for acupuncture, 0% for NSAIDs], they were slightly inferior to those obtained by acupuncture for neck pain [42% vs 50% for acupuncture, 0% for NSAIDs].[171] These results were later found to be sustained for most patients at 1-year of follow-up.[172]

4] Dose-response characteristics:

Until recently, an area of outcomes evidence lacking meaningful documentation pertained to two highly practical areas of chiropractic practice: [i] how many treatments at what frequency produces an optimal effect; and [ii] are the effects enhanced by including ancillary treatments to the manipulative procedure that is at the core of chiropractic treatment? This void has been largely fulfilled by a recent study by Haas, who demonstrated that, regarding spinal manipulations for low back pain, the beneficial effects for both pain and disability continue to accrue for up to 12 patient visits within a 3-week period. These results were apparent at both 4 weeks following the initiation of chiropractic treatment and at 12 weeks. Furthermore, the extended benefits at 12 weeks of follow-up were experienced **only** if ancillary physical medicine interventions were included with the manipulative treatments [**FIGURE 7**].[173]. Therefore, such techniques as hot and cold applications, electrical muscle stimulation, and ultrasound may very well exert a synergistic effect in enhancing and extending the benefits of spinal manipulation. Previously, these physical medicine methods had been judged to be ineffective when used in isolation.[5] Furthermore, the study indicated that, for at least some low back pain patients, cessation of treatment before 12 treatments are completed may be premature.[173]

This study has profound implications in reestablishing the limitations that may have been imposed upon chiropractors by third party payors. It also demonstrates that multifaceted rather than one-dimensional approaches in treating back pain may be in the patient's best interest.

5] Early vs late intervention, preventive SMT:

An important part of the overall planning for the optimum frequency of chiropractic adjustments is the timing of the first intervention. One randomized trial which shed light upon this question involved the randomized assignment of 102 patients with acute low back pain into treatment groups which stipulated a combined treatment of manual therapy, exercise, and biopsychosocial education in one cohort and a waiting period involving no treatment for the other. As might be expected after 6 weeks, the group which was actively treated displayed superior outcome scores relating to disability, mood, general health, and quality of life. At longer terms of follow-up, pain and disability scores of the two groups converged while mood, general health, and quality of life remained superior in the treated group. The implication in this investigation was that an early intervention regimen including manual therapy offers better outcomes.[174]

In terms of prevention, two studies involving elderly populations have been provided. As part of a comprehensive geriatric assessment program, the RAND Corporation studied a subpopulation of patients who were under chiropractic care compared to those who were not and found that the individuals electing continuing chiropractic care were:

*Free from the use of a nursing home [95.7% vs 80.8%];
*Free from hospitalizations for the past 23 years [73.9% vs 52.4%];

*More likely to report a better health status;
*More likely to exercise vigorously;
*More likely to be mobile in the community [69.6% vs 46.8%].[175]

More suggestive data concerning prevention comes from a recent study of patients with chronic low back pain who were divided into two groups, one receiving 12 treatments within a single month and the other adding to this regimen one treatment every 3 weeks for an extended 9 months [12-14 additional visits]. In terms of disability [as indicated by a modified Oswestry questionnaire], the group receiving the supplementary maintenance treatments continued to improve throughout the entire 10 month period, while the cohort lacking the additional visits reverted to baseline levels within that same period.[176] The authors of this study speculate that repeated chiropractic visits may have been the direct cause for the improvement of disability scores due to [a] improved trunk mobility,[177] [b] facilitated release of entrapped synovial folds or relaxation of hypertonic muscle by sudden stretching,[178] or [c] the disruption of articular or periarticular lesions.[179] It is important to emphasize that this particular study addresses supportive [tertiary maintenance] care as opposed to primary maintenance care.

6] Pediatrics research:

Despite the wealth of studies regarding low-back pain outcomes in adult populations[180] and the fact that low back pain is the condition most frequently associated with chiropractic care,[181] there have been no controlled trials to date on the outcomes of chiropractic treatment for low-back pain in pediatric and adolescent populations, according to searches on MEDLINE from 1987-2006 and MANTIS from 1992-2006. From this undertaking, only one cohort[182] and three case studies[183-185] involving spinal manipulation by a chiropractor could be identified.

This gap in the pediatric low back pain literature fortunately has begun to be addressed with a more recent prospective study of consecutive pediatric patients with low-back pain seeking treatment from randomly selected chiropractors within the cities of Calgary, Alberta and Toronto, Ontario, Canada. Chiropractors were eligible to participate if they were in practice for a minimum of 5 years and saw a minimum average of two pediatric patients per week. A maximum of 5 consecutive cases between the ages of 4 and 18 with a new episode of mechanical low back pain [not previously treated by a chiropractor] were accepted. Low back pain was defined as pain or discomfort in the area bounded by the lowest set of ribs in the patient's back to the lower edge of the buttocks. A total of 15 chiropractors provided data on 54 patients, 61% of which were acute presentations and 47% relating to the onset of a traumatic event. All patients were followed until they reported resolution of the problem, discharge, referral, or discontinuation of treatment. Assessment of low back pain was accomplished by means of two indices: [i] the visual analog scale [VAS], and [ii] a subjective 5-point Likert scale. The mean VAS upon presentation was 5.6.

The most commonly used form of intervention was spinal manipulation, with 95% of follow-up visits including this therapy. Included in additional treatments were passive

manual therapy, such as soft tissue treatments and mobilization and such modalities as interferential current and ultrasound. Just 7.7% of patients underwent active management, such as patient-directed home exercises, nutrition, and other education.

Within a 6-week course of management, "much improvement" [Grade 4 on the Likert scale] was attained in 62% of the patients, with a median time of 16 days. "Important improvement"" [Grade 3.8 on the VAS] was reported from 87% of the patients with a median time of 28 days. Patients with chronic low back pain were less likely to respond within the median number of treatments.[182]

Given the fact that chronic patients were less likely to respond and that relatively few practitioners employed

active management strategies, it appeared to the authors that further education of chiropractors regarding this particular mode of treatment was indicated. Because there was no natural history comparison group, it is not possible to directly implicate cause and effect from this particular study. However, there does seem to be a clear implication that the majority of pediatric patients with low back pain [especially acute] respond positively to chiropractic treatment.[182]

The case studies, all addressing lumbar disc herniation experienced by adolescents, require our further attention. All support a prudent course of healthcare, beginning with the most conservative and least invasive modalities and progressing until a positive outcome is attained.[183-185] A study by Hession described a progression from flexion-distraction to side-posture manipulation, with full recovery experienced by 8 weeks with no recurrence of complaints by 16 months after treatment.[183] Kazemi depicted a far more involved and lengthy course of treatments--all conservative--for 20 weeks, yielding a patient who was pain-free at one year of follow-up.[184] King's report described an adolescent who began treatment conservatively [even with a return referral from a neurosurgical consultation] but ultimately underwent surgery for disc removal after just 3 weeks of visits to both chiropractic and allopathic providers.[185] Taken together, these three case studies cannot establish cause-and-effect but do provide a blueprint as to how pediatric musculoskeletal conditions might best be managed by both the chiropractic and allopathic communities. It is also clear that further clinical research including the more controlled design of randomized clinical trials would add invaluable evidence to further support the chiropractic care of pediatric and adolescent populations with back pain.

Despite the multiplicity of outcome studies for adults[186-190] which have gained recognition in a study conducted by Duke University and endorsed by the Agency for Health Research and Quality,[191] there have not been formally constructed manipulation outcome trials with pediatric populations. Rather, there have been numerous case studies and case series, a portion of which have appeared in the peer-reviewed journals. Tension-type, cervicogenic, and even migraine headache have been described with positive outcomes.[192-197] Lisi's investigation is noteworthy in that it reports that the cervicogenic headache frequency decreased to just twice a month *after only a single treatment*.[197]

Other than Hewitt's positive case report,[193] no published outcome studies pertaining to neck and shoulder pain specifically in children could be located. For the present, the encouraging results of the adult clinical trials[156-161] can be interpolated and melded with the aforementioned positive pediatric case outcomes[192-197] to suggest that spinal manipulation in the treatment of pediatric headaches enjoys a modest base of evidence.

7] Lumbar disc herniation research:

Regarding disc herniations, it has been shown that more than a third of total health care and societal costs may be attributed to 1-2% of low back pain patients who undergo surgery for disc herniation.[198] Compared to outcomes of patients undergoing conservative care for disc herniations, surgical patients were found to improve just as rapidly and completely as experienced by a randomized clinical trial,[199] and even more rapidly and completely if seen through the lens of an observational study.[200] The striking results of the latter study speak to the possible importance of **patient expectations** in non-blinded, nonrandomized selections of therapy; however, they must also be interpreted with caution due to the possible confounding of results in self-reported nonrandomized studies.[200] What must be kept in mind is that lumbar disk surgeries have been reported to have a complication rate of 24%, almost half of which are major in nature.[201]

Two randomized trials currently support the wisdom of considering spinal manipulation as a treatment option for this condition. One study involving 51 cases of myelographically confirmed disc herniation compared
rotational mobilization to conventional physical therapy [e.g., diathermy, exercise, and postural education]. The manipulation group demonstrated greater improvement in range of motion and straight leg raising compared to the physical therapy cohort, leading Nwuga to conclude that manipulation was superior to conventional treatment.[202]

The second trial examined 40 patients with unremitting sciatica diagnosed as due to lumbar disc herniation with no clinical indication for surgical intervention. Subjects were randomized into two treatments: [i] chemonucleolysis [chymopapain injection under general anesthesia] and manipulation [15-minute treatments over 12 weeks, including soft tissue stretching, low-amplitude passive maneuvers of the lumbar spine and the judicious use of side-posture manipulations]. Back pain and disability were appreciably lower in the manipulated group at 2 and 6 weeks with no improvement or deterioration in the chemonucleolytic group. By 12 months there were improvements in both groups with a tendency toward superiority in the manipulated co-hort.[203]

Further support for manipulation in the treatment of disc herniations is provided from several prospective studies.[204-208] The largest involved 517 patients diagnosed with lumbar disc protrusion, 77% of these having favorable response from pain after manipulative therapy.[207] A literature review from Cassidy[209] suggests that an additional 14

of 15 patients with lumbar disc herniations experienced significant relief from pain and experienced clinical improvement after a 2- to 3-week course of side-posture manipulation.

2. Neck pain research:

a. The RAND Appropriateness Study: Manipulation and Mobilization of the Cervical Spine:

As it had for the low back pain study, the RAND Corporation conducted both a literature review and a multidisciplinary panel appropriateness study for cervical spine, headache, and upper extremity disorders. With regard to the cervical spine, the RAND literature review suggested that short-term pain relief and enhancement of the range of motion might be accomplished by manipulation or mobilization in the treatment of subacute or chronic neck pain; literature describing acute neck pain was regarded as scanty[210] and remains abbreviated to this day.

As in the earlier low back study,[152-155] the appropriateness of chiropractic cervical spinal manipulation was assessed by an expert multidisciplinary panel, rating an array of more than 1,400 clinical scenarios for appropriateness of chiropractic intervention. In the final ratings, panelists rated 41% of all conditions as appropriate and 43% as inappropriate for chiropractic with disagreement on only 2% of all conditions.[211]

b. Other studies:

Leaping ahead from the RAND study to the most current assessment, a special Neck Pain task force recently commissioned by the Bone and Joint Decade [2000-2010] conducted a critical review of the literature published between 1980 and 2006 to assemble the best evidence associated with neck pain and related disorders. Regarding noninvasive intervention strategies, 359 relevant papers were retrieved with 170 accepted as scientifically admissible. For neck pain excluding whiplash, [i] manual and supervised exercise interventions, [ii] low-level laser therapy, and [iii] possibly acupuncture were regarded as more effective than no treatment, sham, or alternative interventions. Regaining function as soon as possible was considered to be a key component of those treatments found to be most effective.[212]

Leading up to this comprehensive review were several intervening studies with a trend toward superiority in patients who experienced spinal manipulation in treatment. A randomized controlled trial conducted in 1993 by Koes revealed that, for subacute and chronic neck pain, the trial receiving the highest rating indicated that, for neck and back complaints together, improvements in severity of the main complaint were larger with manipulative therapy than for physiotherapy; for neck complaints only, the mean improvement in the main complaint as shown by the visual analog scale was slightly better for manipulative rather than physical therapy.[213] A trial authored by Cassidy one year earlier, studying 100 subjects with unilateral neck pain with referral into the trapezius, revealed that immediately after the intervention, 85% of the manipulated group and 69%

of the mobilized group reported pain improvement. The decrease in pain intensity was more than 1.5 times greater in the manipulated group.[214] Improvements of 44% in the visual analogue scale and 41% in head repositioning

were apparent in the manipulated group in a randomized clinical trial conducted by Rogers, as opposed to the respective values of 9% and 12% in the control group. The author suggested that there may be a possible effect of manipulations on proprioception in patients with chronic neck pain.[215]

Other trials failed to attribute superior effects to high-velocity spinal manipulation per se. Although improvements were observed, differences between the two interventions [chiropractic; physiotherapy] specified in the Skargren study[216] or between the three interventions [chiropractic; physiotherapy, intensive training] used by Jordan[217] could not be detected.

Yet the overall trend toward improvement with manual therapy as a whole in research conducted over the past 15 years is unmistakable. Hoving demonstrated in a trial with 183 patients that manual therapy which employed passive movements, specific articular mobilization, coordination, or stabilization techniques yielded advantages over matched 6-week treatment regimens which specified physical therapy [exercise therapy, manual traction, stretching, massage, heat or interferential current] or continued care by general practitioners.[218]

Against a cohort of chronic neck pain patients given a comparable examination without intervention, a group of individuals with the same condition who experienced a pragmatic regimen of 15-25 chiropractic treatments over a 5-week period yielded significantly lower pain scores with greater head repositioning accuracy. The conclusion was that chiropractic care including high-and low-velocity amplitude techniques, myofascial release, and spine-stabilizing exercises could be effective in reducing pain of cervical origin--as well as proprioceptive sensibility.[219] The keyword here may be "chronic," for it has been found in recent systematic reviews that the literature supporting the effectiveness of spinal manipulation in managing *acute* neck pain remains limited[220] or inconclusive,[221] while if chronic patients are included the level of evidence rises to "moderate" if [i] manipulation or mobilization are compared to general practitioner care for short-term pain reduction of pain, [ii] mobilization is compared to care from a family physician or physical therapist.[221]

Considering the role of exercise, a clearly beneficial effect could be shown in one systematic review when it was coupled to manipulation or mobilization. Distinct benefits could be demonstrated in one group of patients receiving this combined treatment against a waiting list control for acute, subacute, or chronic mechanical neck disorders with regard to pain reduction, improvement of function, or global perceived effects. No such superiority could be seen if exercise was omitted.[222] A trend toward improvement by adding exercise to spinal manipulation could also be seen in one randomized clinical trial involving treatments over 11 weeks.[223]

c. Whiplash research:

The problem facing both diagnosticians and victims facing whiplash is that most moderate to severe cases are invisible upon standard medical examination. As elusive as the "smoking gun" might be regarding this condition, it involves a broader array of soft tissue, neurological, and temporomandibular joint problems than presumed only a decade ago.[224] In Quebec alone, the fact that whiplash in 1989 accounted for 20% of all traffic injury insurance claims with an average compensation period of 108 days[225,226] led the Quebec Task Force on Whiplash and Associated Disorders to conclude that "neck pain is to the automobile what low back pain is to the workplace."[227]

The elusiveness of a definitive, reproducible pathology for whiplash-associated disorders [WAD] have often led the legal and insurance communities as well as the medical to erroneously conclude that there is no physical or organic basis for the symptoms of WAD. This has produced charges of malingering or litigation
neurosis on the part of the patient, leading to the overlaying of psychosocial factors which have only compounded the problem.

Because WAD has been such an elusive target, the work of the Quebec Task Force has not been able to escape criticism. Freeman[228] has raised several objections to the Task Force Guidelines, including the following:

1. Near total elimination of relevant literature: The fact that 99.994% of all articles were eliminated before consideration raises a strong possibility that instructive as well as useless data were discarded.

2. Arbitrary recommendations: In the resulting absence of literature to consider, the Task Force gave its own opinion equal weight with primary research data, lending a misleading sense of robustness to its recommendations.

3. Propagation of the myth that most WAD patients recover in 6-12 weeks: Upon closer examination, this time course has no basis no primary research; in fact, considerable data already cited contradicts this impression and paints a far bleaker picture.[229-236]

4. The undertaking was sponsored by an insurance industry: SAAQ [Societe d'assurance automobile du
Quebec] as the sponsoring organization of the entire project would be expected to have an "obvious and serious" interest in its outcome, possibly compromising the objectivity of the literature research,
evaluation, and ultimate recommendations of the Task Force.

From a morphological point of view, immobilization of the neck following the soft tissue

trauma which accompanies WAD is indefensible. Severe soft tissue injury [rupture of muscles, joint capsules, and synovial folds] can be expected around the cervical spines of accident victims.[229] Consequently, scar formation, cross-linking of collagen fibers, and adhesions might be expected to result in traumatized soft tissues that were not rehabilitated soon after injury. Specifically:

1. Healing without proper motion will cause a disorganized matrix to appear, with adhesions and unnecessary scar formation.[231,232]

2. Early exercise and joint motion in rehabilitation produces a better collagen concentration, which is superior to scar tissue.[232]

3. Improved tensile strength is observed in the collagen deposit when proper rehabilitation takes place after injury.[233,234]

4. If venous blood supply to para-spinal muscles is depressed for 2 hours [which might be anticipated in some soft tissue injuries], irreversible muscle damage occurs.[235] With decreased vascularization, rapid degeneration of the muscle spindles occurs--with subsequent revascularization changing their shape and neural innervation.[236]

One would thus conclude that a plausible rationale exists for managing whiplash by spinal manipulation; however, the outcomes evidence in support of this remains limited. One study demonstrated that, in subjects whose side bending of the neck was asymmetrical and who had a history of neck trauma and frequent episodic neck stiffness, a single lower cervical adjustment delivered to the side of the most restricted movement was capable of reducing the extent of asymmetry, but only briefly (for periods less than 48 hours).[237] A second investigation involving 93 patients in a retrospective review by structured telephone interviews indicated that those with restricted range of neck movement following whiplash injury were the most likely to improve after chiropractic manipulation. Many patients had received previous treatments, particularly physiotherapy.[238] Additional supporting evidence might be inferred from a prospective study of 23 patients with subacute whiplash-associated disorders who reported an increased cervical range of motion and reduced pressure-pain threshold after cervical spine adjustments,[239] as well as one case study involving an unstable C3/C4 motor segment following a lateral-impact motor collision.[240]

However, more recent systematic literature reviews have been mixed in their findings. The aforementioned Bone and Joint Decade Task Force on Neck Pain and Its Associated Disorders concluded that educational videos, mobilization and exercises seem to be more beneficial than usual care or physical modalities.[212] On the other hand, another systematic search from various databases from January 2000-May 2006 accepted only 9 studies out of 290 screened and concluded that, because of vague and inadequate explanation of results in several instances, that there was not enough evidence to suggest that spinal manipulation is an effective treatment for whiplash.[241]

3. Headache research:

The treatment of headaches with spinal manipulation has generated a proliferation of research in the peer-reviewed literature, reflected in part by multiple outcomes research designs. At least 13 randomized clinical trials have been reported,[186,242-254] the remainder being case series, retrospective series, or prospective series.[255-265]These have been amply summarized by five literature reviews,[266-270] four of them systematic.[266-269] Additional basic research which will be addressed below[271-274] describes a possible mechanism of cervicogenic headache and as such provides compelling support to the wisdom of considering chiropractic intervention as a key strategy for the management of headaches.

Published studies have generally classified headaches into three major groups, as recommended by the International Headache Society.[275]

a. Tension Headache:

The most dramatic of the trials pertaining to tension headaches[186] was published in 1995. A group of 70 patients who were administered chiropractic health care over a 6-week period displayed parity to a cohort of 56 patients who were administered amitriptyline [a leading medical intervention for headache treatment] over the same period, in terms of four primary outcome measures [headache frequency, total headache pain, OTC medication use, and global health]. More significantly, during the 4-week follow-up period, patients undergoing spinal manipulation maintained their improvements while medicated patients reverted to baseline values [**FIGURE 8**]. What this result implied was that spinal manipulation rather than one type of medication had the potential of conferring benefits to headache patients that were more long-lasting. Of profound importance is the fact that this particular study was rated the highest in quality of all trials compared in the three independent systematic literature reviews mentioned earlier.[266-268]

The enhanced consequences of chiropractic management in the treatment of tension headaches is supported by two other randomized controlled trials,[243,244] although sample sizes were smaller so as to blunt the statistical analyses of these particular results. High-velocity thrusting did not seem to confer additional benefits upon patients given massage and trigger-point therapy, as shown in one other trial by Bove and Nilsson.[245] Even though this particular investigation would suggest that *high-velocity thrusting* confers no additional benefits for managing tension headache, it is clear that both groups of patients which had been administered massage [an arguable component of chiropractic management] showed significant and indistinguishable improvements over baseline values in all the outcome measures observed. The danger of misinterpretation arises when chiropractic healthcare is equated with only one of its elements [high-velocity manipulation].

Outcomes obtained in nonrandomized clinical research are similarly supportive. Mootz reported improvements in frequency, intensity, and duration in 11 patients subjected to cervical manipulation, cold packs, and trigger point therapy.[255] Droz, on the other hand,

witnessed improvements in pain in a large cohort of 332 patients administered spinal manipulative therapy.[256]

b. Cervicogenic Headache:

Cervicogenic headache is defined as pain originating in the cervical spine and referred to the head.[275,276] Studies pertaining to cervicogenic headache are at least as compelling. In comparing patient groups given either high-velocity cervical spinal manipulation or low-level laser treatments as a control, Nilsson observed improvements of the manipulated group in terms of pain experienced, headache hours per day, and use of analgesics to alleviate discomfort. Statistically significant recoveries in all categories [analgesic use, frequency, intensity] were obtained with those patients subjected to high-velocity adjustments, even though both the control and experimental groups had been subjected to massage.[246] Nilsson's investigation speaks eloquently to the importance of employing large enough groups to achieve statistical significance, since his own earlier report had shown merely a statistically insignificant *tendency* toward improvement since the experimental and control groups of patients were not large enough.[247] A less astute investigator would have become victimized by what is known as a Type II error by accepting the results of the earlier research as Gospel.

An additional clinical trial comparing patient groups subjected to either 9 active upper cervical or toggle recoil adjustments or sham manipulations demonstrated 28-36% reductions in headache frequency, duration, severity, and medication consumption. No such improvements were observed in the placebo group.[248]

Yet another randomized clinical trial by Jull split 200 cervicogenic headache participants into four groups receiving [i] a Maitland low-and high-velocity protocol for manipulative therapy, [ii] a low-load endurance exercise regimen, [iii] combined manipulative and exercise therapy, and [iv] a control treatment. Each active intervention showed a significant reduction in frequency, intensity, duration, and neck pain as compared to the control with effect sizes being moderate and clinically relevant.[249]

Following much the same design as described earlier (**Section IV.B.1.b.4])** in measuring dose-response effects, Haas and his coworkers randomly allocated 24 adults with cervicogenic headache into groups visiting a chiropractor 1,3, or 4 times per week over a 3-week period. All patients received high-velocity, low-amplitude manipulations plus up to two physical modalities including heat and soft tissue therapy at the discretion of the attending chiropractor. Substantial benefits in pain relief were seen at 4 and 12 weeks for those groups receiving 9 and 12 treatments as compared to 3, demonstrating that continuing treatments for up to 9-12 treatments conferred additional benefits to at least some groups of patients.[250]

Further supportive evidence from nonrandomized clinical research was offered by Vernon. In a prospective series of 33 patients, he found reductions of frequency and intensity following spinal manipulation.[257]

c. Migraines and Unclassified Headaches:

The earliest randomized clinical trial involving spinal manipulation of patients with migraine headache was conducted over 40 years ago and revealed no significant differences in migraine frequency, duration, or induced disability between patient groups receiving [i] manipulation by a chiropractor, [ii] manipulation by a medical practitioner or physiotherapist, or [iii] mobilization by a medical practitioner or physiotherapist. However, the chiropractic cohort did report a greater reduction of pain associated with the attacks.[251] Using a very similar design to that utilized in his investigations with tension headache,[186] Nelson observed analogous results in his clinical trial involving patients with migraine headache. There was no advantage to combining amitriptyline and spinal manipulation for treatment. Clinically important improvements were observed in all 3 study groups over time, but once again during the follow up period, significant differences emerged--with reductions of the headache index amounting to 24% for the amitriptyline group, 42% for spinal manipulation, and 25% for the combined group.[252] By comparing manipulation to detuned ultrasound for treating migraine patients in another clinical trial, Tuchin reported statistically significant improvements in headache frequency, duration, disability, and medication use.[253] In his study of unclassified post-traumatic headache, Jensen compared cold packs with mobilization in a third clinical trial and demonstrated a reduction of pain by 43% in

the manual therapy population compared to the cold therapy group at two weeks following treatment.[254]

Two nonrandomized clinical research designs provided additional evidence supporting the efficacy of spinal manipulation in managing migraine headache. In a series of 87 patients, Wight observed reductions of pain;[258] Stodolny reported reductions of pain and dizziness and improvements in range of motion in a series of 31 patients.[259]

d. Pediatric headache:

Despite the multiplicity of outcome studies for adults just described above, there have not been formally constructed manipulation outcome trials with pediatric populations. Rather, we find numerous case studies and case series, a portion of which have appeared in the peer-reviewed journals. Tension-type, cervicogenic, and even migraine headache have been described with positive outcomes.[261-265] Lisi's investigation is noteworthy in that it reports that the cervicogenic headache frequency decreased to just twice a month *after only a single treatment*.[265]

e. Basic Research: The Myo-Dural Bridge:

As pointed out earlier [**Section III**], not all research evidence which supports the wisdom of a particular healthcare intervention comes to us from outcomes research. Sometimes a clarification of what appears to be an underlying mechanism provides an invaluable

complement to effectiveness studies observed in traditional clinical trials. Nowhere is this more evident than in the recent discovery from direct tissue dissections of what appears to be a connective tissue bridge between the rectus capitus posterior minor muscle [RCPM] and the dorsal spinal dura at the atlanto-occipital junction.

According to Gary Hack and his coworkers, the dura-muscular connection transmits forces from the cervical spine joint complex to the pain-sensitive dura. Trauma to the upper spine could then result in atrophic changes in the RCPM. Consequently, adverse tension in the spinal dura could further substantiate the role of spinal manipulation as a means to alleviate this tension and offer valuable support to the effectiveness of SMT as a viable treatment for cervicogenic headache.[271] These structural relationships are demonstrated in **FIGURE 9**.[272]

Support for this model is shown in a parallel study in which 31 out of 39 consecutive patients who underwent plastic surgical forehead rejuvenation procedures encompassing resection of the corrugator supercilli muscle displayed total elimination or improvement of migraine headache, with improvements lasting at least 47 months.[273] Thus it is quite possible that various types of headache are at least in part triggered by tension of various muscular bridges, the relaxation of which [presumably by spinal manipulation] could bring about substantial relief from the original complaint. The idea that such a multiplicity of muscular bridges exist is supported by the findings of Humphreys, who demonstrated the existence of the ligamentum nuchae in addition to the rectus capitus muscle, anchored between the occipital bone and the C1 vertebra.[274]

f. The Duke Headache Evidence Report:

To verify the clinical outcomes evidence supporting spinal manipulation and a variety of other physical and behavioral interventions in the management of headache, the Agency for Health Quality and Research began a process of systematic review of the literature that was virtually identical to that completed with the release of guidelines pertaining to low back pain, as discussed earlier.[5] Unfortunately, funding cuts to the agency caused this process to be aborted after the headache literature review had begun, and the work of the multidisciplinary committee charged with performing the literature evaluation and developing ratings of the evidence was ultimately shipped to the Duke Center for Health Policy Research and Education for safekeeping.

It was at this juncture in which I, with funds from the National Chiropractic Mutual Insurance Company, was able to mandate that an updated systematic literature review of tension and cervicogenic headache be done, taking into account the rapid proliferation of new literature to be grafted onto the work of the disbanded headache committee. This new undertaking led the staff at the Duke Center to screen citations from the literature, abstract the data into evidence tables, analyze the quality and magnitude of results from these studies, and draft an evidence report with peer review from a panel of 19 experts representing a broad, multidisciplinary coalition of healthcare providers.

Starting with over 2500 citations from such sources as MEDLINE, MANTIS, CRAC, CINAHL, PsychoINFO, the Cochrane Controlled Trials Register, and additional articles obtained by referral, the panel obtained bibliographies of both physical and behavioral options for treating headache which were either prospective, controlled trials aimed at either relief from or prevention of attacks of tension-type or cervicogenic headache. Among the physical interventions reviewed in this report were: [i] cervical spine manipulation, [ii] low-force techniques [such as cranial sacral therapy, massage (including trigger point release)]; [iii] mobilization; [iv] stretching; [v] heat therapy; [vi] ultrasound; [vii] transcutaneous electrical nerve stimulation (TENS)]; [viii] surgery; and [ix] exercise (including those that are postural]. Among the behavioral interventions reviewed were: [i] relaxation; [ii] biofeedback; [iii] cognitive-behavioral [stress management] therapy; and [iv] hypnosis.

The final report, which gave copious recognition to much of the chiropractic research headache literature cited earlier,[242-270] was significant in that it concluded that non-pharmacological treatments are of growing importance and, "if effective and available...[they] may be the first choice for most patients." Furthermore, it indicated that drug treatments are not suitable for all patients, may produce undesired side effects. and are not universally effective.[277] The importance and high credibility of this document lay in the facts that [i] Duke is one of 12 research centers given trademark status by the U.S. Department of Health and Human Services, [ii] the 19 member interdisciplinary panel that performed the literature review was of extremely high caliber, and [iii] the evidence review was comprehensive--encompassing all behavioral and physical treatments for both tension-type and cervicogenic headache.

4. Extremities:

Manipulation of the musculoskeletal system for treatment of pain and reduced motion is not limited to the back or neck. Over the past decade, the extremities have become increasingly recognized as an area responsive to manual therapy. This is supported by reports which indicate that upper and lower extremity problems account for up to 20% of all chiropractic care, half of which pertains to lower extremity pain and injury.[278-282] Indeed, the treatment of extremities is the second most frequently applied procedure within the chiropractic profession.[278]

a. Upper extremities:

The shoulder girdle, for example, may be amenable to such treatment. One clinical trial in The Netherlands randomized 150 patients with shoulder symptoms and dysfunction were randomized into groups receiving either usual medical care [information, oral analgesics, NSAIDs, corticosteroid injections, referral to physiotherapy] or high-velocity low-amplitude manipulations in addition to the medical regimen over a 12-week period. After 12, 26 and 52 weeks, distinct advantages in the manipulated cohort were reported in severity of the main complaint, shoulder pain and disability, and general health. The conclusion was that spinal manipulation accelerated the recovery of shoulder symptoms.[283]

Compression of the median nerve within the vicinity of the wrist may lead to unilateral or bilateral paresthesia in the fingers, with or without pain in the wrist, palm, and/or forearm proximal in the area of compression. This condition, known as carpal tunnel syndrome [CTS], presents a variety of symptoms and is commonly confused with tendinitis. One of its major causes is the protracted strain on an extended or flexed wrist caused by repetitive stress, often found in the workplace and therefore having the potential to affect a significant population.

The rationale for manipulation is to take pressure off the transverse carpal ligament and add adjustments of the lunate to help decompress the tunnel. It represents a departure from traditional spinal adjustment; in its application to the extremities instead, it provides a conservative, noninvasive alternative to surgery.[284]

A systematic review of upper extremity conditions performed on the CINAHL, MEDLINE and MANTIS databases yielded 64 articles, including 6 clinical trials, 14 case reports for the wrist and hand, 8 case reports for the elbow, and 36 case reports involving the shoulder. Although the level of evidence overall was judged to be extremely modest, what was most striking was that the chiropractic treatment was multimodal in nature, involving both the spinal and peripheral structures and using both joint and soft tissue methods. This was judged to be at odds with the general perception of other healthcare providers that chiropractors employ mostly manipulative methods of treatment.[285]

Although few in number at the present, the randomized clinical trials addressing CTS offer encouragement in that discrete improvements in a broad cross-section of outcome measures [physical and mental distress scores, nerve conduction, vibrometry, and pain scores] in patients compared to their initial conditions are noted in all groups undergoing manipulative therapy. Their improvements were comparable to those achieved by ibuprofen[286] physical therapy or corticosteroid injection.[287] In the latter trial plus one additional investigation,[288] manipulative therapy displayed the potential to accelerate improvement in certain groups of patients,, although corticosteroid injections produced more rapid improvements in patients with diagnosed disorders in synovial structures as opposed to functional disorders of the cervical spine, upper thoracic spine, or the upper ribs [the shoulder girdle].[288]

Case series designs addressing manipulative therapy for carpal tunnel syndrome have also yielded encouraging results. A series of 22 volunteers screened for CTS by electrodiagnostic characteristics, symptoms, and physical examination received either manual soft tissue mobilization or soft tissue mobilization assisted with Graston instruments. Improvements to 3 months were observed in nerve conduction latencies, wrist strength, wrist motion, and subjective evaluations of signs and symptoms of CTS.[289] A second cohort of volunteers at least 60 years of age who suffered from upper extremity [hand, wrist, or shoulder] dysfunction experienced manual manipulation, mobilization, and ancillary treatments [soft tissue procedures, McKenzie physical therapy assessment, application of ice and heat, treatment with home stretching, postural exercises] 1-3 times

per week over a 5-week period and reported improvements in self-reported pain and functional status.[290]

Case control studies supporting chiropractic intervention in the management of this condition suggest that, in 38 subjects, a broad array of dietary, exercise, and manipulative interventions result in statistically significant improvements in several strength measures of up to 25% over pretreatment values;[291] improved objective pain and distress levels were observed in 22 returning subjects to persist for at least 6 months post-treatment.[292]

Osteopathic manipulation has also been shown to be effective in two case series studies by Benjamin Sucher. The first, involving four patients with CTS, showed both clinical improvement and changes in MRI imaging that revealed that the anteroposterior and transverse dimensions of the carpal canal increased significantly after treatment. EMG/NCS measurements were able to document electrical improvement consistent with the clinical recovery.[293] Both clinical and electrical improvement were subsequently observed in a larger group of 16 patients with CTS.[294]

b. Lower extremities:

Two extensive literature reviews regarding manipulative therapy and the lower extremities have recently been published, one by Hoskins[295] and the other guided by the conclusions of the Council on Chiropractic

Guidelines and Practice Parameters [CCGPP] and being more limited by defining *chiropractic treatment* using applied manipulative therapy with or without adjunctive treatment.[296] The CCGPP study was particularly comprehensive with its inclusion of randomized controlled/clinical trials, case series, and case studies, as well as in its judicious weighing of the implications of such features as the introduction of innovative concepts or insights, or the absence of intention-to-treat analyses.

In the 39 studies [8 for the knee, 7 the ankle, 2 the foot, and 1 the hip] reviewed in the CCGPP study, levels of evidence were judged to be "fair" if (a) there were studies of appropriate design of sufficient strength, but
there were inconsistencies or minor doubts about generalizability, bias, design flaws, or the adequacy of sample size, or (b) the evidence was gleaned from weaker designs but confirmed in separate studies.

Evidence was "limited" if there were either (a) studies with substantial uncertainty due to design flaws or adequacy of sample size, or (b) a limited number of studies of weak design for answering the question addressed. Brantingham and his coauthors concluded that the evidence was "fair" for manipulative therapy of the knee and/or full kinetic chain, and or the ankle and/or foot combined with multimodal or exercise therapy for knee osteoarthritis, patellofemoral pain syndrome, and ankle inversion sprain. Evidence was deemed to be "limited" for manipulative therapy combined with multimodal exercise therapy for hip osteoarthritis.[296]

This was not to be construed as a discouraging result, as Brantingham concluded overall that "the present studies for lower extremity disorders appear to parallel the results and overall beneficial outcomes per spinal research."[163,228] Indeed, the table has been effectively set for a broader consideration of what constitutes the musculoskeletal disorders amenable to chiropractic care, for the author has suggested that "it may be useful to investigate the most effective methods of manipulation/mobilization for *every joint in the human body* [italics mine]."[296]

C. Non-musculoskeletal:

1. Observed as a "by-product":

An early systematic indication that non-musculoskeletal as well as musculoskeletal conditions were responsive to chiropractic care came from a study of 87 Swedish Chiropractic Association members, each of whom surveyed 20 consecutive adult patients whose chief complaint was musculoskeletal in nature. Treatments included a spinal adjustment or manipulation. What was found was that 23% of these patients reported at least one positive benefit which extended beyond the musculoskeletal system, the most common involving the respiratory and digestive systems. The percentage of individuals reporting non-musculoskeletal improvements increased steadily with the number of spinal areas treated.[297]

These findings were confirmed and extended by an international research consortium, which extracted data from 385 chiropractors and 5,607 patients from 7 countries [Canada, United States, Mexico, Hong Kong, Japan, Australia, and South Africa] in a cross-sectional survey, revealing similar proportions of chiropractic patients originally seeking treatment for a musculoskeletal condition who reported improvements in non-musculoskeletal complaints after treatment. Similar to the preceding Swedish study, most common were improved breathing [27%], digestion [26%], circulation [21%], and resolution of tinnitus [19%].[298]

2. Infantile colic:

First described in 1894 as dyspepsia, infantile colic has most recently been described as the unexplainable and uncontrollable crying in babies aged 0-3 months for more than 3 hours per day, more than 3 days a week, and more than 3 weeks. Some studies have described flexing of the knees against the abdomen with clenching of the fists and extension of the trunk or extremities.[299]Although the condition has been regarded to be self-limiting and benign, its effect upon parent-child relationships can be construed to be stressful if not damaging.

To buttress years of promising clinical observations, a number of interventions have recently been conducted [**TABLE 8**][299-305] with results forover 450 patients that are mostly supportive. All involve chiropractic spinal manipulation applied either by fingertip or a

computer-assisted solenoid adjusting device. What is most dramatic is the comparison shown with a medical treatment--the surfactant dimethicone [**FIGURE 10**]--which not only produced a considerably lesser effect from 5-10 days after the start of treatment, but produced worsening of symptoms as was apparent in 7 of the medicated group of patients.[299] While the effects of manipulation compared to a hand-held placebo group did not appear to differ statistically in one study by Olafsdottir, a trend toward superiority in the numbers of patients affected is apparent. Furthermore, more of the manipulated group indicated "some" or "marked" improvement.[300] Elsewhere, a pilot randomized clinical trial suggested that the complete resolution of symptoms could be found in 93% of the subjects undergoing up to 6 treatment sessions over a 2-week period.[301] What remains a matter of mystery is whether Olafdottir[315] adjusted areas of the spine that were different from those manipulated in the other randomized clinical trials, possibly accounting for the divergent results.

While spinal manipulation is usually associated with the treatment of musculoskeletal disorders, these data create two possible interpretations. As indicated by Wiberg,[299] either spinal manipulation has been shown to be effective in the treatment of a visceral disorder or infantile colic is, in fact, a musculoskeletal disorder rather than the visceral condition it is commonly assumed to be. In either case, these data provide further support for considering the use of spinal manipulation in treating specified pediatric conditions.

3. Enuresis:

This condition has been described as having multifactorial origins.[306] It has been proposed that spinal joint dysfunction could disrupt the integration of somatic, spinal, parasympathetic and sympathetic nerve pathways--constituting a significant contribution to the patient's enuretic condition. Thus, clinical studies that have appeared in the literature involving over 200 patients,[307-310] suggest that spinal manipulative therapy may play a role in managing this condition [**TABLE 9**]. The results of the randomized clinical trial[307] are difficult to ignore.

While the majority of cases did not appear to respond in one of the studies,[308] it was felt that more information could have been obtained in the presence of a control group given a sham procedure in a randomized controlled trial. In that particular study, the manipulated group did indeed display a significant improvement over its own baseline values while the placebo group did not. However, the mean pre- to post-treatment night frequency group for the test group compared with that of the control group was not quite statistically significant at the 5% level.[308] A larger sample size would most likely have created a statistically robust difference between the groups. In addition, despite its minuscule n of 1 design, Gemmell's study displayed a time-series improvement following manipulation which defied the natural course of improvement.[310]The remaining case study also reported significant improvement.[309]

4. Asthma:

The typical control of asthma by medication is primarily through antiinflammatory agents

[inhaled steroid or beta-2-agonists [bronchodilators], the last of which when used excessively may actually contribute to an increase of mortality and morbidity.[312] There has thus been a shift toward using anti-inflammatory agents; at the same time, questions have been raised as to whether alternative and less invasive means are available for controlling this condition.

Spinal manipulation has been proposed as an option for treating this specific condition primarily for two reasons. The first is that vertebral dysfunctions assumed to underlie chiropractic management could produce reflex irritations of the somatic and autonomic nervous system; second, from both a neurological and biochemical point of view, chest wall function or bronchial airway tone and/or responsiveness might be expected to be adversely affected by such a lesion--leading to a increased risk for an asthmatic attack.[313]

Reduction or elimination of these joint aberrations might thus be expected to reduce the incidence of asthmatic events.

In addition to descriptive or anecdotal data which have reported a positive clinical effect of spinal manipulation for asthma,[314,315] four randomized clinical trials plus a pilot, three cohort studies, one crossover investigation, and four case studies involving over 550 patients as shown in **TABLE 10** offer measurable support for spinal manipulative therapy in the management of this condition.[113,316-328] Lung function improvements per se may not be detectable,[316,319] but quality of life scores improved by 10-28%, led by activity scale changes.[319] The largest randomized clinical trial to date which is attempting to compare different manipulative techniques in the management of asthma is currently underway in Australia. Although data on symptoms**,** quality of life and distress are forthcoming in this study, preliminary cortisol measurements indicate that with manipulation [as opposed to patients visiting but remaining untreated], cortisol levels decrease.[113] Immunoglobulin A levels, on the other hand, specifically increase in treated asthmatic patients. These results are noteworthy in that prolonged elevations of cortisol have been shown to be potentially life-threatening [including being a cardiovascular risk factor[110,329]], leading to the development of bronchial hyper responsiveness and asthma.[330]

The apparently negative study appearing in The New England Journal of Medicine, stating that "the addition of chiropractic spinal manipulation to usual medical care for four months had no effect on the control of childhood asthma," requires further comment. This statement was based upon the failure of active and sham-manipulated patient groups aged 7 to 16 years to be differentiated in terms of their outcomes in both quality of life and airway function. What is indisputable is that there were major improvements from baseline to follow up observed in each of the groups.[316] The problem arises when one considers what was actually done in the sham procedures. Prolonged applications to no less than 3 distinct anatomical areas [gluteal, scapular, cranial] to the patient were described. Admittedly, these were not high-velocity contact procedures, but this appears to obscure an important phenomenon. Two pieces of evidence strongly suggest that

simple contact with patients through sham procedures may produce significant effects in terms of asthma relief. The first indicates that, with respect to the reflexive inhibition of the alpha-motor neuron pool in human subjects, sham and active manipulative procedures display little difference. This is to suggest that cutaneous receptors, muscle spindles, and joint mechanoreceptors individually or in concert are significantly affected by so-called sham procedures.[95] The second arises from studies of Field from the University of Miami, in which low-force massage as opposed to *no contact* with the patient was sufficient to elicit differential, beneficial responses in overcoming asthma symptoms, lowering anxiety scores, and reducing cortisol levels.[115] This more than anything else should indicate that physical contact with the patient is sufficient to trigger a cascade of physiological changes which Balon erroneously dismissed in his asthma study.

In this context, the reader must take note that chiropractic extends beyond high-velocity, low-amplitude adjustments. It encompasses a broad range of both high-velocity and low-force techniques together with ancillary procedures, many of which have obviously been embedded in the sham procedures described. In its attempt to craft a fastidious design, the Balon trial[316] appears to have missed the forest for the trees by attempting to portray the essence of chiropractic care as the lack of differentiation between the sham and manipulated experimental groups.

A contrast between sham and experimental interventions is apparent in the osteopathic literature inasmuch as thoracic function tests display a difference between sham and active procedures in a crossover design.[321] Reductions in the use of medications are apparent after manipulations from the reports of several cohort and case studies.[322-325,328]

5. Dysmenorrhea/Premenstrual Syndrome:

For over 250 patients, the outcome studies shown in **TABLE 11** point out marked improvements in menstrual pain and distress associated with dysmenorrhea and premenstrual syndrome.[122,123,127,331-334]

Particularly noteworthy are the results from the pilot study performed by Kokjohn, which indicated clear improvements for patients subjected to higher manipulative forces in a side-posture procedure. Here it was evident that such patients experienced reductions in pain and their menstrual distress survey scores as well as significant decreases of the prostaglandins associated with menstrual cramping. In this manner, both clinical outcomes and a physiological mechanism (as discussed above in section **III.E.**) were clearly associated with the high-velocity chiropractic intervention and not the sham procedure.[122]

The apparently negative outcome in one of the full-scale trials[123] is easily explained by a myriad of irregularities in its design. The problems begin with the eligibility requirements of patients, which in the larger study were relaxed in order to attain sufficient recruitment. The result was that patients were sometimes admitted having experienced no pain within the past 48 hours and did not have to forego exercises or NSAIDs for a blackout period

prior to the trial, in contrast to what had been required in the pilot study which had far stricter admission requirements.[122] In the latter trial, only a single practitioner delivered sham and active treatments and, not surprisingly, the experiment delivered positive results[122] as opposed to the lack of significant differences between the treatment and sham groups in the full-scale trial.[123] The fact that multiple therapists delivered sham and active treatments with no confirmation of standardized training or uniformity of application of thrusts represents yet another liability of the full-scale trial. Taken together, the flaws in the larger study are of such a magnitude as to invalidate the entire study.

Less rigorous support for the effectiveness of manipulation in managing dysmenorrhea is offered in the remaining pilot investigation [127] as well as the randomized comparative study, the latter providing a different chiropractic technique.[334] For treating premenstrual syndrome, the supporting evidence is more tenuous but uniformly encouraging.[332-334]

6. Otitis media:

Otitis media is the term used to describe the inflammation of the middle ear, the region between the ear drum and the outer ear. Although still lacking a randomized clinical trial, a substantial body of evidence exists to support considering chiropractic intervention for managing otitis media. To begin, such standard medical treatments as antibiotics and tympanostomy tubes have been shown to have limited applications, serious complications, and in the case of antibiotics have often been irrationally prescribed.[335-338]

TABLE 12 outines the results of large cohort and case studies for over 850 patients**,** offering support for the effectiveness of chiropractic or osteopathic manipulative therapy for treating this condition.[339-347] It can be seen that the majority of otitis media cases treated with spinal manipulation appear to be resolved within 10 days, most responding to fewer than 5 adjustments[342-344] and many requiring only one or two treatments.[342,343] Particularly intriguing is the fact that patients with no history of prior ear discomfort were much more likely to show early improvement, avoiding the cost and time of further interventions.[342] Normalization of otoscopic and tympanographic results likely occurred more quickly in cases of acute rather than chronic otitis media as shown in two studies.[342,343] Fewer surgeries and episodes of acute otitis media were also encountered by patients undergoing osteopathic manipulative treatments.[339] Mastoiditis [the chief complication of otitis media] occurs only 0.2-2% of the time, even without antibiotic treatment;[348] it behooves the physician to consider not only chiropractic spinal manipulation as a treatment option for otitis media, but as a possible *first* alternative in light of the more rapid responses achieved in acute cases.

7. Hypertension:

A list of studies involving nearly 475 patients affected with hypertension undergoing spinal manipulation is provided in **TABLE 13**. Two each of randomized clinical trials, pilot studies, crossover designs, nonequivalent comparisons, case series, and case studies plus one cohort study often reveal significant decreases in blood pressure measurements,[131-134,137,349-356] One of the most dramatic decreases in both systolic and

diastolic pressure [13 and 8 mm, respectively, at week 8] has recently been reported by Bakris for a low-force chiropractic intervention described as the

oNational Upper Cervical Chiropractic Adjustment [NUCCA]. The rationale for this approach was that looping arteries at the base of the brain were observed in one study to lead to arterial compression of the left lateral medulla oblongata in 51/53 hypertensive patients. When vascular decompression of the medulla was performed in 42 of the 53 patients, a reduction in hypertension was observed in 76% of them. By changing the position of the Atlas vertebra by means of the NUCCA technique, effecting such a decompression, it was held that reductions in blood pressure would ensue. This hypothesis was borne out in that both substantial reductions of blood pressure and rotational displacements of the Atlas vertebra [the restoration of alignment] immediately followed NUCCA treatments. Of considerable importance are the facts that [a] 85% of the patients treated required only a single adjustment, and [b] the effects persisted throughout the 8-week duration of the study.[134]

Because there was no variation of heart rate, it was proposed that changes in sympathetic tone were not responsible for the changes in blood pressure observed.[134] On the other hand, one of the principal drivers of blood pressure--serum aldosterone--was observed to decrease in one of crossover studies;[133] however, the actual blood pressure effect was extremely brief. The failure to register sustained lowerings in a few of the studies[133 137,350] might be attributable to the technique applied or the severity of the condition.

8. Heart rate variability:

Linkages of spinal dysfunctions to cardiac function can be traced to the observations of Jarmel,[358] who drew from several sources in the literature suggesting that prevention of sudden cardiac death should be directed toward controlling neurophysiologic factors which could enhance ventricular vulnerabilty.[359-362] One source of destabilizing neural input to the heart was proposed to be vertebral dysfunction, the correction of which could be of value in reducing susceptibility to sudden cardiac death.[358] Because spinal manipulation was suggested to relieve the neural irritation caused by vertebral dysfunction,[363,364] the use of such an intervention for preventing or forestalling the events leading to cardiac mortality became a subject for further study. In particular, decreased heart rate variability in response to stress was linked to greater risks of mortality.[361]

What is intriguing is that heart rate variability (HRV, the analysis of beat-to-beat oscillations in heart rate) was once thought to be merely noise in an electrocardiogram.[365] But using a Fourier mathematical analysis, it was possible to translate the oscillations into frequency ranges,[365,366] measured either within a 24 hour period using time domain statistical analysis or short-duration recordings of 5 minutes using frequency domain statistical analysis. A complete description as to how HRV can calculate a qualitative index of autonomic function, accurate reflecting the sympathetic and parasympathetic tone and sympathovagal balance, has been provided, with low frequencies (LF) linked to sympathetic activity.[367,368]

HRV outcomes following spinal manipulation have been demonstrated with 60 patients, primarily with crossover randomized clinical trials (**TABLE 14**). Increases of frequency ranges which are indicative of greater sympathetic output to the heart were shown following either cervical (C_2)[97] or thoracic[98] manipulation by Budgell. The same result was demonstrated in 3 patients by Welch in the thoracic region. Inexplicably, a *decrease* in LF activity, suggesting a relative *increase* in parasympathetic activity, was found by the same author after manipulations in the cervical region.[99] While opposing effects of manipulation regarding sympathetic and parasympaethic nervous system activity appear to be linked to manipulations of different regions of the spine, this particular finding needs to be repeated with a substantially larger cohort of patients before its apparent divergence from the results of Budgell[113] can be taken up in detail.

The remaining case study shown in **TABLE 14** was not able to come to definitive conclusions regarding the power analysis of HRV. However, the establishment of more uniform heartbeats and the disappearance of trigeminal pulses which appeared in the electrocardiogram are noteworthy.[369]

9. Case study support:

As has been noted in **TABLES 8-14**[298-300,309,310,325-328,334,345-347,355,356,369] and in more recent and progressive literature reviews,[296,370] the results of case studies have often served as a beacon for guiding future, more rigorous clinical research designs. That said, numerous non-musculoskeletal conditions not previously described or studied with larger numbers of patients have been reported to respond to spinal manipulative therapy. These are shown in **TABLE 15**,[371-379] hopefully to guide larger clinical investigations in the future. In so doing, these case studies would have performed the same function as those which motivated all the studies previously described in this report pertaining to both musculoskeletal and non-musculoskeletal conditions.

D. Cognitive changes:

Changes in the nervous system, as discussed above in **Sections III.D.** and **IV.C.8.,** have implicated that alterations in central nervous system processing take place after spinal manipulation. This would be expected to affect both somatosensory transmission[93] and motor control.[380] A prospective double-blind randomized controlled trial involving 36 chiropractic students attempted to determine if cortical processing, as shown by response times to a mental rotation reaction-time task, is altered by spinal manipulation. After one high-velocity, low-amplitude upper cervical adjustment, subjects displayed an average decrease in mental rotation reaction times of 98 ms, equivalent to a 14.9% improvement. The effect was specific in cognitive processing as distinct from improving movement time by the fact that following adjustments there was no significant change a simple reaction-time task which required a minimal amount of cortical processing. The evidence suggested that upper cervical adjustments may affect cortical processing.[381]

A similar experiment involving 10 patients aged 24-46 from a private chiropractic practice involved moving a cursor onto a target appearing on a computer screen. The experimental group, which had one high-velocity, low-amplitude adjustment to areas of joint dysfunction, registered improvements of about 9%. The control group, undergoing a resting period after completing a baseline task, displayed only a 2% improvement. The validity of this observation was compromised by the fact that the control group consisted of only a single patient. Yet the implication, again, seemed to be that a spinal adjustment could influence motor behavior and/or cognition.[382]

V. Safety

A. Major complications: Relative risks of activities:

A number of studies have linked chiropractic manipulation to adverse events, the most serious and widely studied being strokes following dissections of the vertebral artery.[383-388] Regarding the risks of cervical manipulation in producing vertebral artery dissections (VADs) several retrospective studies against large population bases have been conducted. As shown in **Table 16**[389-397], a large sampling of such studies indicate that the number of serious complications or cerebrovascular accidents (CVAs) as established by researchers from both the chiropractic and medical professions ranges from 1 case per 400,000 manipulations to zero in 5 million. Data from the RAND Corporation suggests the rate of vertebrobasilar accident or other complications [cord compression, fracture, or hematoma] to be 1.46 per million manipulations, with the rates of serious complications and death from cervical spine manipulation estimated to be 0.64 and 0.27 per million manipulations, respectively.[266] A more recent retrospective review, involving the largest number of presumed cervical manipulations performed [134.5 million] over the longest period of time [10 years], used malpractice claims from the Canadian Chiropractic Protective Association. It revealed a total of 43 cases of neurological symptoms retrieved from patient records, 23 of which involved stroke. The total yield of strokes, therefore, was 23/134.5M, a frequency rate of 1 per 5.85 million [0.17 per million] cervical manipulations, equivalent to one stroke per 1430 chiropractic practice years or a stroke occurrence rate of one per 48 chiropractic practice careers.[396]

The risk estimates attributed to cervical manipulation are significantly less [by orders of magnitude] than those associated with various medical procedures and lifestyle activities as shown in **Table 17**.[266,398-404] In an exhaustive review of risk estimates from multiple phases of life, Rome points out that the substantially greater
risks attributed to the medical procedures have been deemed "acceptable" by the routine adoption of such terminologies as "risk-adjusted mortality rates" and "net clinical benefits." The problem becomes all the more ironic in that, in Rome's words, "there seems a reluctance to concede the application of these terms outside the medical profession."[405] The risks inherent in other lifestyle activities, also appearing to be readily accepted by the public at large, are apparent in **Table 17** and again outweigh those associated with cervical manipulation by several orders of magnitude. In striking contrast

to the dire media warnings about the risks of cervical manipulation in the media.[406-411]

B. Study of the vertebral artery and artery wall:

1. Structural considerations:

The vertebral and basilar arteries, comprising the vertebrobasilar system, supply blood to the posterior brain. The vertebral artery (VA) itself, emerges from the subclavian artery, passes through the transverse foramina of C_6 – C_1 to become the atlantal segment as it exits through the transverse foramen of C_1. It is here that the atlantal segment abruptly bends from a vertical to horizontal orientation. It is at this juncture (**Figure 11**) at which the artery is believed to be most susceptible to injury related to sudden and/or extreme head movement.[412] Three layers from inside to out (tunica intima, tunica media, tunica adventia) comprise the cervical arteries, as shown in **Figure 12**.[413]

2. Mechanisms of dissection:

As the layer which makes up the vessel lining, the tunica intima is more susceptible to tearing[413] and as such is the typical site of the initial defect which initiates a VAD. A typical developing dissection as shown in **Figure 13A** indicates the formation of an intimal flap following an initial tear, with the potential for the separation of layers caused by blood flowing into the breach. Further damage may be wrought by pulsatile pressure to the muscular layer causing further splitting of the intima and media during a dissection. Subintimal hemorrhaging may rupture back into the arterial lumen distally, creating a double (false) lumen (**Figure 13B**). As blood accumulates within the separated vessel layers, a thrombus is created with further deformation of the intima and obstruction of blood flow (**Figure 13C**). If emboli detach from the primary thrombus, they may travel distally to block progressively smaller vessels in the brain (**Figure 13D**).[413]

Perhaps the most compelling information that needs to be brought forward to bring the debate about cervical manipulations into objective terms has to do with the fact that a significant number (and most likely the majority) of VADs happen to be spontaneous cervical artery dissections (sCADs). Numerous reports to be discussed below, addressing both the frequency of occurrence of VADs and their association with virtually any activity associated with turning the head, should reduce the utility of attributing strokes to cervical manipulations to virtually an academic exercise.

As shown in **Table 18**, the annual incidence of spontaneous VADs in hospital settings has been estimated to occur at the rate of 1-1.5 per 100,000 patients[414] The corresponding VAD incidence rate in community settings has been reported to be twice as high.[415,416] Using an estimated value of 10 from the literature to represent an average number of manipulations per patient per episode,[417] it becomes apparent that the proposed exposure rate for CVAs attributed to spinal manipulation is equivalent to the spontaneous rates for cervical arterial dissections as reported.[414-416] If the threat of stroke or stroke-like symptoms is to be properly assessed, therefore, at least half our attention needs to be directed toward the spontaneous events instead of primarily or solely upon

spinal manipulation.

Furthermore, a large number of common lifestyle activities have been shown to be associated with cerebral ischemia [**Table 19A**][405] or VADs themselves [**Table 19B**].[418] All are decidedly non-manipulative. By way of illustration, one recent investigation has described beauty parlor stroke syndrome and salon sink radiculopathy confirmed by both patient symptoms and blood flow velocities in the bilateral vertebral and carotid arteries as measured by a diagnostic ultrasound instrument.[419]

3. Role of homocysteine, its detection, and means to reduce its effects:

For over 30 years, the amino acid homocysteine has been implicated as key component of atherosclerotic disease.[420-428] More direct observations point toward the disruption of the structures of collagen and elastin in the arterial wall:

1. In the majority of skin biopsies taken from patients with cervical arterial dissections, irregular collagen fibrils and elastic fiber fragmentations have been found.[429]

2. Homocysteine activates metalloproteinases[429] and serine elastases,[430] directly or indirectly leading to the decrease in-vitro of the elastin content of the arterial wall. The opening and/or enlargement of fenestrae in the medial elastic laminae would be expected to lead to the premature fragmentation of the arterial elastic fibers and degradation of the extracellular matrix.[429,430]

3. Homocysteine has been shown to block aldehydic groups in elastin, inhibiting the cross-linking needed to stabilize elastin.[431]

4. The cross-linking of collagen may also be impaired by homocysteine.[432]

5. Experimentally elevated levels of homocysteine produce patchy desquamation of 10% of the aortic surface in baboons.[426]

6. Endothelium-dependent and flow-mediated vascular dilation is impaired in individuals with elevated levels of homocysteine.[428]

7. In cell culture experiments, addition of homocysteine into the medium induces cell detachment from the endothelial cell monolayer.[433]

Yet even a tighter coupling between sCADs and increased amounts of homocysteine have been shown by the following observations:

1. Patients undergoing sCADs are more than three times as likely as asymptomatic patients to yield plasma homocysteine levels exceeding 12 micromoles/L. They are also

more than twice as likely to have elevated homocysteine as patients experiencing ischemic strokes *without* arterial dissection.[434]

2. CAD patients yield average homocysteine levels of 17.9 micromoles/L while asymptomatic patients report an average of 6.0 micromoles/L.[435]

3. Homocysteine levels exceeding 10.2 micromoles/L are associated with a doubling of vascular risk.[420]

4. A genetic defect in humans involving tetrahydrofolate reductase, the enzyme which produces the methyl-donating cofactor required to convert homocysteine to methionine, is associated with elevations of the rates of sCADs.[434] This metabolic block would be expected to cause homocysteine to accumulate intracellularly.[436]

The striking association of homocysteine with sCAD raises the possibility that a relatively simple diagnostic test is at hand for determining patients at risk for sCAD and who would accordingly be advised to avoid cervical manipulation. Until recently, the gold standard methodology for determining plasma homocysteine has been high pressure liquid chromatography, gas chromatography and mass spectrometry.[437-439] Fortunately, this cumbersome technology has recently been correlated with a much simpler enzyme conversion immunoassay [EIA].[440] An even more rapid assay method by means of an automated analyzer is also available, requiring only microliter amounts of reagent and sample.[441] This essentially means that homocysteine levels can be determined in any number of clinical reference laboratories already established to measure blood analytes.

To date, the assessment options for vertebrobasilar artery risk each have significant drawbacks and as a whole have been unable to identify any particular factor that is useful for screening.[442,443] Provocation tests in particular are problematic in that in several aspects they replicate the risks associated with cervical manipulation by requiring the placement of the head and neck in extreme extension and rotation[444] False negative findings compared to angiograms have been reported;[445] reliability and validity have not been reliably tested;[443] and the suggestion has been made that these tests be de-emphasized.[446] In the midst of this disorder, determining homocysteine levels as a predictor of arterial fragility seems to be a plausible, rapid and inexpensive procedure that is no more invasive than a routine blood glucose determination.

A more extensive discussion of spontaneous arterial dissections, the proposed involvement of homocysteine, and means to determine homocysteine clinically has been published elsewhere. In addition, there is evidence presented to suggest that homocysteine levels may be lowered by folate, raising the possibility that a commonly available vitamin might be of utility in forestalling or preventing a potentially life-threatening condition.[60]

C. Linking cerebrovascular accidents to manipulation:

1. Risk factors:

Although symptomatology of neck pain may mimic that of an incipient or ongoing VAD, the primary signal of arterial distress is a sudden onset of headache or neck pain which patients often report is unlike any experienced previously. Signs and symptoms of actual vertebrobasilar ischemia which should be regarded as further suggestions of an impending vertebrobasilar artery event are:[447]

*Diplopia or other visual problems
*Dizziness: vertigo or lightheadedness
*Drop attacks
*Dysarthria
*Dysphagia
*Ataxia of gait
*Nausea, possibly with vomiting
*Numbness
*Nystagmus

When considering a patient for neck manipulation, a number of risk factors should be weighed carefully before treatment is considered:[447]

*Dizziness, unsteadiness, giddiness, and vertigo
*Age <45
*Migraine
*Connective tissue disease:
  >Autosomal dominant polycystic kidney disease.

  >Ehlers-Danlos Type IV
  >Marfan Syndrome
  >Fibromuscular dystrophy
*Recent infection, particularly upper respiratory

2. Other adverse events:

Despite numerous reports which have suggested that spinal manipulation is capable of causing disk herniations and cauda equina syndrome (CES),[448-451] estimates of the frequency of such events arising from spinal manipulations performed for any reason range from 1 in 1 million[405,451] to 1 in over 100 million.[157,452] A more recent systematic review of prospective and retrospective studies as well as review papers yielded a risk estimate of worsened disk herniation or CES to be less than 1 in 3.7 million, **three to five orders of magnitude less** than such accepted means of treating lumbar disk herniations as the use of NSAID medications or surgery.[453]

More minor and transient events attending chiropractic manipulation have been reported in the literature. These have been of short duration, relatively infrequent, and rarely severe. A sampling of such incidents includes:

*Increased neck pain or stiffness[454]
*Headache and radiating pain[455]
*Lightheadedness, dizziness, fainting (incidence 16/1000)[397]
*Headache, numbness, tingling in upper limbs (incidence 4/100)[397]
*Severe headache (case reports, pediatric)[455]
*Mid-back soreness (case reports, pediatric)[455]
*Musculoskeletal soreness[456]
*Tiredness, nausea, ringing in ears (incidence <8%)[456]

3. Flaws in the medical literature:

While much of the medical literature attempts to establish an association of spinal manipulation with adverse events,[382-388] it fails to fulfill the basic principles of causality established over 40 years ago by Bradford Hill.[457] What is required to demonstrate true epidemiological causation is the satisfaction of all the following:

1. Strong associations with a diagnosis which is consistent across samples and groups
2. Temporal relationship of treatment and adverse event
3. Biological plausibility
4. Lack of conflict with alternative explanations
5. Demonstration that reduced exposure to the putative causal agent results in reduction or prevention of the adverse event.

In terms of the most severe events--the VADs--seven common flaws can be identified in the bulk of the medical literature which attempts to link VADs with spinal manipulation:

1. There is the failure to disclose that the majority of VADs are spontaneous, cumulative, or caused by factors other than spinal manipulation (**Table 18**).
2. There is the failure to disclose the potential benefits of the procedure, as must be done in reporting true risk-benefit ratios.
3. There is the failure to place the risks of manipulation in the context of those produced by other medical treatments or lifestyle activities (**Table 17**).
4. There is the failure to report the actual frequency of spinal manipulations administered.

5. There is the failure to account for the possibility that patients experiencing CVAs are reported more than once.
6. There is the failure to report the rates of CVAs following manipulation by parties other than licensed chiropractors.[418,447,458]
7. There is the blanket assumption that patients undergoing adverse events following a

manipulation would fail to report such instances to either the attending chiropractor or appropriate authority.

The one major omission in numerous case-control studies which suggested that the incidence of strokes was greater in patients who had recently undergone spinal manipulations by a chiropractor compared to individuals who had not[387,388] has thankfully and finally been addressed. In a study of 818 VBA strokes in a hospitalized population of over 100 million person-years, Cassidy and his coworkers demonstrated that strokes were just as likely to occur if patients with headache or neck pain visited a primary care physician rather than a chiropractor, suggesting that the cause of the stroke could not be plausibly associated with any element unique to chiropractic. More likely, the stroke was already in progress when any healthcare intervention was sought.[459]

To amplify this point even further by way of demonstration, a recent case control study of a patient with a non-traumatic episode of head and neck pain revealed the benefits of taking a careful case history before ordering any intervention. Here it was found that the patient displayed sufficient warning signs to warrant a delay in administering spinal manipulation. Within a week of watchful waiting, the patient experienced a CVA anyway. Again the implication was that factors resulting in a stroke were in progress at the time the patient first sought consultation from a healthcare practitioner.[460]

VI. Cost-Effectiveness Research

A. Rationale:

Given that rising healthcare costs in America now consume 16% of the Gross National Product and that their inflation of nearly 8% in 2004 was almost triple the overall national inflation rate,[461] cost-effectiveness is clearly a major factor in assessing the capacity to deliver effective healthcare. When it comes to managing back pain as the leading condition treated by chiropractic, we are faced with daunting statistics when it comes to cash outlays. According to the 1998 Medical Expenditure Survey, for instance, it was shown that total health care expenditures for back pain were $90.7B, more than 15% of which represented the costs of prescription drugs.[462] In terms of spine care, annual expenditures rose 65% from 1997 to 2005 while the health status of individuals with spine problems failed to improve, indicating that the money invested in this pursuit was not returning a sufficient value.[463] And in terms of neck pain, no form of surgical surgery has been shown to be superior to nonsurgical care or watchful waiting.[464] Finally, Dr. Richard Deyo's comment on back pain has clearly raised a red flag concerning conventional care:

"Calling a physician a back-pain expert, therefore, is perhaps faint praise--medicine has at least a limited understanding of the condition. In fact, medicine's reliance on outdated ideas may have actually contributed to the problem."[465]

Consequently and fortunately, there is a body of research one can focus upon when it comes to the cost-effectiveness of chiropractic care.

B. Methodological concerns:

Typically, initial chiropractic visits including a complete medical evaluation, diagnosis and treatment. Numerous comparisons have been made with the costs which would be encountered in visits to a medical physician. Here it is essential to note that most costs for chiropractic visits are *included* in the bill received

from the chiropractor's office, whereas in the medical course of treatment, external costs such as [i] referrals to medical specialists including physical therapists, [ii] the purchase of medications, and [iii] laboratory tests, most costs from the medical provider per se are not. In actual figures, it has been shown that 80% of the total cost of chiropractic treatment is billed from the chiropractor, whereas only 20% of the total medical costs of treatment appear on bills directly from the medical physician.[466] Even though the total number of visits to a chiropractic office for treating a given episode may be numerous, therefore, the patient needs to be mindful of this accounting.

To begin with appraisal of cost-effectiveness studies, one must assess the minimal criteria and common deficiencies of cost-effectiveness studies. In reviewing cohort studies in occupational low back pain, Baldwin identifies 6 requirements:[467]

1. The sample must be identified immediately after the onset of pain.
2. The study must obtain data on the prior history of back pain.
3. Standardized outcomes measures must be collected.
4. The total costs of an episode of back pain must be measured accurately.
5. Costs must be evaluated from the viewpoint of a pre-identified payor.
6. Multivariate models must be used to control for patient differences.

Looking at the other side of the coin, Branson has cited 5 common *deficiencies* in investigations pertaining to cost-effectiveness:[468]

1. Patient characteristics (severity, chronicity) are not factored in.
2. Standardized diagnoses within or between providers is not controlled in retrospective studies.
3. Payments actually received as not the same as those billed.
4. There is an absence of all direct costs, such as (a) all visits to the provider, (b) prescription and nonprescription drugs or supplements, (c) laboratory costs, (d) diagnostic imaging, (e) referral to specialists, and (f) hospital costs.
5. There is a poor representation of *indirect* costs, such as (a) workdays lost by the patient, (b) retraining for replacement labor, (c) caregivers to assist in domestic duties, (d) iatrogenic events, and (e) legal costs.

C. Leading types of studies:

1. Workers' Compensation Data:

Attention is immediately drawn as to how healthcare dollars might have been inappropriately spent for back pain in workers' compensation from disbursements recorded, in which benefits were disbursed by the State of Georgia to medical and chiropractic physicians from 2001-2004 according to the data shown in **Table 20**:[469] Here it can be seen that chiropractors received 1% or less of the funds paid to medical physicians and just 2.8-4.5% of the disbursements paid to physical therapists. Since low back pain has been proposed to represent 33% of all workers compensation costs and 16% of all workers compensation claims,[470] it is immediately apparent that chiropractic care may not represent a significant cost burden as suggested by such entities as the Workers Compensation Research Institute in their overall conclusions.[471,472] Indeed, one of the major methodological concerns which compromises the data from the latter study group is that costs of providers other than chiropractors were split into separate categories, whereas all costs relating to chiropractors were bundled into a single entity.[471,472]

Recent retrospective data from the Division of Workers' Compensation Claims in Florida revealed drastic savings when chiropractic was compared to non-chiropractic care for specific low back injuries during the period 1994-1999. Here total costs per claim were less than half for chiropractic care ($7,500 vs $16,500); the average time required to reach maximum medical improvement was 37% less (161 vs 219), and the average number of days required to return to work was reduced by 30% as well (77 vs 130). Incredibly and

most shocking was the fact that, during this same period, utilization of chiropractors for such injuries decreased by 75% with at most only a 15% reduction of the number of cases treated by non-chiropractors.[473]

Much the same pattern was found in Texas. In this instance, the authors retrieved over 70 articles, reports, published studies, and treaties on the costs and effectiveness of chiropractic care and analyzed data on nearly 900,000 Texas Workers Compensation Claims from 1996-2001. Here chiropractors treated 30% of workers with lower back injuries but accounted for just 9.1% of the total costs and 17.5% of the medical costs,[474] mimicking the previously discussed results from Georgia[469] representing the disproportionately low benefits apportioned to chiropractors.

These same trends persisted in the state of North Carolina, in which a retrospective review of 96,627 claims between 1975 and 1994 archived by the North Carolina Industrial Commission produced the same compelling and ultimately unsettling data. Here it was shown that the treatment costs, total costs, and total time of disability for medical providers was $3,519, $17,673, and 176 days, respectively. The corresponding figures for chiropractic care, on the other hand, were just $663, $3,318, and 33 days. Just as shown previously,[469,474] the utilization rates for medical (85.4%) and chiropractic (0.8%) providers were far from equal.[475]

Oklahoma yielded similar findings, in which a 41% savings in direct costs with expanded

access to chiropractic care for lower back sprains and strains was demonstrated. In actual amounts, these savings translated to $14,190,011 annually.[476]

Similar findings could be extracted from studies overseas. Ebrall's study of the Victorian Work Care Scheme in Australia from the early 1990s matched 998 medical with an equal number of chiropractic claims for patients with mechanical low-back pain and found that the number of compensation days was 392 when the provider was a chiropractor and 774 when the provider was a medical practitioner. The average compensation payment was four times greater with medical management ($1,569 vs $392).[477] Similar data from the Work Cover Authority in a neighboring province (New South Wales) during the same period revealed that the average chiropractic treatment cost for 20 randomly selected cases was $299.65, less than half the $647.20 average medical treatment cost per case.[478]

2. Databases from insurers and practitioners:

Insurance companies often use larger databases, which are less prone to possible skewing by regional workers' compensation data. The challenge still exists however, that problems remain for all retrospective studies in that all claims filed require verification to be certain that they correspond to the actual conditions experienced and treatments rendered.

Several earlier studies from Utah,[479] Iowa,[480] and Florida[481] provided preliminary data which suggested a significant savings in costs when chiropractic was compared to medical care for back problems. Perhaps even more important was the fact (often neglected in cost-effectiveness studies as suggested above) that days lost from work were significantly less for patients under chiropractic care.[479-481] Other early data from Oregon suggested that chiropractic care was more expensive and prolonged.[482]

A key conceptual advance representing the bundling of the full costs of episodes (i.e., the careful inclusion of all relevant treatment costs, not solely the costs of out-patient doctor visits) associated with either the medical or chiropractic care of patients was accomplished by Stano. Factoring in key patient demographic and insurance characteristics as well as case mix severity differences, Stano ran final cost comparisons in a total of 6799 patients from a total database of over 400,000. His conclusions were straightforward and dramatic. When all episodes of care were considered, the mean total costs were $1000 for each medical episode and $493 per chiropractic episode.[483]

Later observational studies by the same author at 13 general medical practices and 51 chiropractic, community-based clinics revealed higher rather than lower chiropractic costs. However, the data were misleading in that (a) the distributions of total costs were highly skewed, especially for the chiropractic group, (b) prescription drug costs from the charts of medical patients may be underestimated, (c) the costs for imaging or referral services rendered or independently sought by patients outside the sample providers'

clinics were not included, (d) a disproportionately high percentage of chiropractic patients (42%) paid out-of-pocket whereas only 7% of medical patients did so, and (e) costs for patients who might have undergone surgery were not considered.[484]

The same authors revisited the issue of cost-effectiveness three years later with a cohort of 2780 patients visiting either 60 chiropractors or 11 medical doctors in their own offices and concluded that, although chiropractic costs continued to be higher, they were more than offset by the fact that clinically important differences in pain and disability improvement were found only in the chiropractic patients. Coupled with greater patient satisfaction and considering the importance of *indirect* costs as discussed above (**Section VI.B**), the authors now concluded that chiropractic care appeared to be relatively cost-effective for chronic patients.[485] The same conclusion regarding quality of life and cost-effectiveness of spinal manipulation was echoed in a much larger study in actual treatment settings in the United Kingdom. [486]

If chiropractors were admitted into an integrative service as gatekeepers in an Independent Physicians' Association (IPA), dramatic cost reductions were observed in several investigations. In a retrospective study over a 4-year period by Sarnat, hospital admissions were reduced by 43% and hospital days were reduced by 58% with the average length of stay cut by 34% when comparisons were made to conventional health maintenance organizations which had not awarded primary care privileges to chiropractors.[487] In an updated study over a 7-year period, the decreased utilization of hospitals, pharmaceuticals, and outpatient surgeries and procedures was sustained by chiropractors compared to medical providers. Actually, decreased utilization of more expensive and invasive medical procedures was uniformly achieved by all primary care providers whose orientation was toward complementary and alternative medicine, regardless of their licensure.[488]

Another perspective was offered by an insurance plan in a 4-year retrospective claim analysis, comparing 700,000 health plan members with an additional chiropractic coverage benefit and 1M members of the same health plan without the benefit. Including the chiropractic benefit resulted in (a) lower annual total healthcare expenditures ($1,463 vs $1,671), (b) lower average back pain episode-related costs for back pain patients ($289 vs $399), (c) a reduction of claims through medical doctors, and (d) lower utilizations of plain radiographs, magnetic resonance imaging, back surgeries, and hospitalizations. The savings were even greater than those reported because all pharmacy costs, costs of physical therapy on referral, and post-surgical patients were omitted. The sheer magnitude of the study group made this one of the largest analyses ever performed on the economic impact of chiropractic; however, it needs to be noted that this study was confined to one health plan in one state and that cause and effect have not been firmly established. Nevertheless, the trends of these data are undeniable.[489]

One corollary of this study was to ask whether adding the chiropractic benefit created an additional demand for medical care services, thereby adding significant costs. An investigative group from the same insurance firm responsible for the previous study[489]

found that the presence of the chiropractic benefit did not appear to increase the number of patients seeking care for neuromusculoskeletal conditions, offering substantial refutation to this argument.[490] A second outgrowth of these investigations was to compute the actual costs of surgery, CT/MRI, plain-film radiography, and surgery for patients with or without the benefit. Those individuals with the benefit incurred reductions of costs in these categories from 2-25% for back pain and 13-31% for neck pain.[491]

In viewing the cost of physician services through the lens of Medicare, similar advantages to chiropractic care could be found. Muse & Associates undertook an examination of the utilization, cost and effects of

chiropractic services on Medicare program costs compared to similar data for beneficiaries treated by other provider types. Using data from a compilation from the Centers for Medicare and Medicaid Services, the study group compared the data from 1.5M who received chiropractic care against the remainder of the 5.8M total who did not. Beneficiaries who received chiropractic care had lower average Medicare payments per capita for all Medicare services ($4,426 avs $8,103), lower average Medicare payments per capita for the treatment of selected conditions ($380 vs $594), and fewer encounters with physicians.[492]

Finally, a more recent study which has captured more of the direct and indirect costs required for a comprehensive cost analysis as discussed above of medical services (**Section VI.B**) was provided in Europe, offering the additional benefit of a "bootstrapping" processing of costs which bypassed the assumptions required for conventional statistical analyses. In this study, patients undergoing manual therapy, physiotherapy, or conventional care from a general practitioner for neck pain were compared in a randomized clinical trial. The total costs of the manual therapy were *one-third* those of the other two groups; in addition, the manual therapy group displayed more rapid improvement in pain intensity, perceived recovery, and quality of life than the medical or physiotherapy cohorts for up to 26 weeks.[508]

D. An economist's evaluation of existing literature:

Pran Manga, an economist at the University of Ottawa, has been twice commissioned by the Provincial Government of Ontario to assess the effectiveness and cost-effectiveness of chiropractic management of low-back pain. His assessment of the comparative cost data in his first report led him to conclude that:

"There is an overwhelming body of evidence indicating that chiropractic management of low-back pain is more cost-effective than medical management. We reviewed numerous studies that range from very persuasive to convincing in support of this conclusion. The lack of any convincing argument or evidence to the contrary must be noted and is significant to us in forming our conclusions and recommendations."[6]

The cost advantages for chiropractic for matched conditions appear to be so dramatic

that Manga, in his second report, concluded that **doubling the utilization of chiropractic services from 10% to 20% may realize savings as much as $770 million in direct costs and $3.8 billion in indirect costs.** Four out of five patients of chiropractors have endured their problems for more than 6 months, typically undergoing medical care and/or physiotherapy before even reaching their chiropractor.[494]

VII. Wellness and Prevention

A. Significance in healthcare delivery:

The reemphasis of healthcare upon preventive services has been widely regarded as essential if America's healthcare system is to survive into the future. The rising costs of healthcare, now exceeding 15% of the gross national product with outcome results which indicate that the United States has far less to show for its healthcare expenditures in terms of longevity and quality of life permit no alternative but to pursue prevention aggressively. A complete overhaul of healthcare delivery involving preventive health measures as an integral part has been strongly recommended in a recent report from the Institute of Medicine of the National Academies.[495] The persistence of public unawareness of the benefits of particular interventions plus the placement of practical obstacles for physicians being able to deliver effective services has been reported by a research group from McMaster University.[496]

B. Recent research:

In terms of prevention and potential l cost savings, two studies involving elderly populations are difficult to

ignore. As part of a comprehensive geriatric assessment program, the RAND Corporation studied a subpopulation of patients who were under chiropractic care compared to those who were not and found that the individuals under continuing chiropractic care were:

*Free from the use of a nursing home [95.7% vs 80.8%];
*Free from hospitalizations for the past 23 years [73.9% vs 52.4%];
*More likely to report a better health status;
*More likely to exercise vigorously;
*More likely to be mobile in the community {69.6% vs 46.8%].

Although it is impossible to clearly establish causality, it is clear that continuing chiropractic care is among the attributes of the cohort of patients experiencing substantially *fewer* costly healthcare interventions.[175] This demands a closer look at the potential advantages of continuing chiropractic care for elderly patients.

A second review of a larger cohort of elderly patients across the United States compared direct expenditures [hospital care, physicians' services, nursing home] between groups of patients who were under maintenance chiropractic care and those who were not. Nearly a threefold savings of mean annual expenditures was reported as follows:

*$ 3,105 : Maintenance care
*$10,041 : No maintenance care[497]

Other studies involving preventive measures for non-elderly populations exist as well. One such investigation reviewed the consequences of implementing an on-site industrial chiropractic program which included the early detection, treatment, prevention and occupational management of musculoskeletal injuries 2 days per week. For the 21 months after implementation of the program, the total number of days of lost time, costs per claim, rate premiums, and especially the number of surgeries decreased dramatically. Cost savings from avoided surgeries alone amounted to $900,000 for these preventive measures.[498]

A second study recruited 59 adults aged 18-27 from two elite Australian Rules football teams and randomized them into intervention and control groups. The control group was administered standard club, medical, paramedical and sports science management, including medication, surgery, manipulative physical therapy, massage, strength and conditioning, and rehabilitation. The intervention group included all these procedures and added pragmatic chiropractic management, involving manual therapies and/or soft tissue therapies to the spine, pelvis, and lower extremities at a minimum weekly frequency for 6 weeks, then one treatment for every 2 weeks for a 3-month period. The chiropractic intervention resulted in the lower incidence of injuries to the hamstrings, lower limb muscles, and knees with far shorter periods of play missed as well. A lower incidence of overall back pain was also reported.[499]

Again the implications are that there may be considerable potential savings in direct costs spent for medical care with patients who are undergoing continuing chiropractic care on a maintenance basis. When return-to-work and other indirect costs are figured in (as implied in the Coulter study described above[175]), far greater savings would be expected.

But perhaps the most persuasive data of all comes from a recent study[176] of patients with chronic low back pain who were divided into two groups, one receiving 12 treatments within a single month and the other adding to this regimen one treatment every 3 weeks for an extended 9 months (12-14 additional visits). In terms of disability (as indicated by a modified Oswestry questionnaire), the group receiving the supplementary maintenance treatments continued to improve throughout the entire 10 month period, while the cohort lacking the additional visits reverted to baseline levels within that same period. This is clearly depicted in the Oswestry scores over a 10-month period as indicated in **Figure 21**. The authors of this study speculate that repeated chiropractic visits may have been the direct cause for the improvement of disability scores due to (a) improved trunk mobility,[193] (b) facilitated release of entrapped synovial folds or relaxation of hypertonic muscle by sudden stretching,[500] or (c) the disruption of articular or periarticular lesions.[501]

VIII. Conclusions

This discussion has attempted to review the position and potential of chiropractic research from a multiplicity of perspectives. It began with a historical review, together with a critical assessment of the state of what is currently called evidence-based medicine. When assessing the rationale for choosing a particular healthcare intervention, this discussion has, in its review of basic research, emphasized the importance of **biological plausibility**, since this turns out to be one of the basic elements of causation as established by Bradford Hill over 40 years ago.[457] Indeed, *without* the insights afforded by research in the basic science fields of molecular biology, microbiology, physiology, biochemistry, genetics, physics, and chemistry as well as anatomy, discoveries which have been of such a benefit to medicine over the past centuries would have been drastically curtailed.

Following a discussion of methodologies, the review of outcomes research was conducted from the viewpoints of both musculoskeletal and non-musculoskeletal disorders which appear to have notable literature supporting the efficacy of chiropractic care in their management. Adhering to the basic tenet in medicine of Primum non nocere (First do no harm), this chapter reviewed a multiplicity of considerations regarding the safety of spinal manipulation, including an expanded discussion as to how a significant proportion of the incidents attributed to manipulation most likely originated from metabolic defects compromising arterial integrity. It became apparent that any risks of spinal manipulation, while remaining an objective which further research and best practices strives to reduce, are orders of magnitude less than those encountered for medical interventions treating the same or similar conditions managed by chiropractic.

In terms of practicality and accessibility of healthcare alternatives, the relative costs of medical procedures relating to conditions most commonly managed by chiropractic care needed to be reviewed. Differing experimental approaches--many lacking attention to indirect costs--were presented and assessed and provide a noteworthy rationale for elevating chiropractic management to a higher priority in the healthcare marketplace.

Finally, to conform with today's necessity to emphasize prevention and the maintenance of good health, instances in the literature in which chiropractic management was found to forestall or prevent further problems, disabilities, or expenses were reviewed. It goes without saying that preventive measures go hand-in-hand with substantially lowering overall healthcare costs.

The role of such research as has been reviewed in this chapter in establishing best practices for any healthcare intervention can never be underemphasized. It is sobering to note, for instance, in a very recent review of guideline recommendations to establish benchmarks for the quality of care in cardiology, Tricoci and his colleagues found that such advisories often rest upon lower levels of evidence or expert opinion. The proportion of recommendations for which there is no conclusive evidence was also found to be growing.[502] If guidelines for such invasive, costly, and procedures with relatively high risks for cardiology exist, one can only imagine that guidelines for conditions with lower mortalities might receive even less scrutiny. This is why the level of research evidence needs to be upgraded and perhaps revisited with more attention devoted to other types of

research besides outcomes, the latter being often the only standard upon which the advisability of a particular mode of healthcare is commonly based. It is hoped that the multiple forms of consideration offered in this discussion provide a meaningful first step in that direction.

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TABLE 1

CLINICAL CARE METHODS: STRENGTH OF EVIDENCE AS DETERMINED BY AHRQ[5]

INTERVENTION	RESULT	STRENGTH OF

EVIDENCE

1. Patient Education		+		C
2. Back School		+		C
3. Acetaminophen	+		C	
4. NSAIDs	+		B	
5. Phenylbutazone	-		C	
6. Muscle Relaxants		+		C
7. Opiod Analgesics		+		C
8. Oral Steroids		-		B
9. Colchicine	-		B	
10. Antidepressants	-		B	
11. Spinal Manipulation		+		B
12. Physical Agents/Modalities[a]		-[b]		C
13. TENS	-		C	
14. Shoe Insoles	+		C	
15. Shoe lifts [Lower Limb diff <2 cm]		-		D
16. Lumbar Corsets/Back Belts		-		D
17. Traction	-		B	
18. Biofeedback		-		C
19. Trigger Point Injections	-		C	
20. Ligamentous/Sclerosant Injections		-		C
21. Facet Point Injections	-		C	
22. Epidural Injections[c] [No Radiculopathy]		-		D
23. Epidural Injections[c] [Radiculopathy][d]		+		C
24. Acupuncture		-		D
25. Limited Activity	+		D	
26. Bed Rest >4 Days		-		B
27. Conditioning Exercise	+		C	

[a]Includes ice, heat [including diathermy], massage, ultrasound, cutaneous laser treatment, electrical stimulation excluding TENS.

[b]Insufficient proven benefit to justify their cost.

[c]Steroids, lidocaine, opioids.

[d]After failure of conservative treatment as a means to avoid surgery.

TABLE 2

STEPS OF EVIDENCE-BASED MEDICINE[14]

STEP	PROCESS
1.	Converting the need for information [about prevention, diagnosis, prognosis, therapy, causation, etc.] into an answerable question [Also known as formulating a clinical question].
2.	Finding the best evidence with which to answer that question.
3.	Critical appraisal of the research evidence for validity, impact, and application.
4.	Integration of the critically appraised research evidence with the expertise of the practitioner and the patient's unique biology, values and circumstances.
5.	Evaluating the effectiveness of the process in improving patient care and practitioner efficiency in executing steps #1-4 and seeking ways to improve both.

TABLE 3

NEURAL RESPONSES TO EXTERNAL FORCES IN ANIMAL MODELS

Animal	Intervention	Effect Observed
Mouse[77]	Ligature implant around sciatic nerve	Inflammation Reduced nerve conduction velocity Facilitation Motor disturbances in gait
Rat[78]	External pressure on L6	Slower nerve conductivity
Rat[36]	Surgical clamp insertion with bending at T10-T11	Decreased blood pressure Decreased renal nerve activity
Rat[79]	Ligature implant around sciatic nerve	Changes in gait Changes in nerve conduction velocity Enzymatic changes in denervated muscles
Rabbit[80]	Manual manipulation	Gastric smooth muscle inhibition
Dog[81]	Surgery plus glue injection into bilateral apophyseal joints in upper lateral spine	Impairment of natural killer lymphocytes
Rabbit[82]	Miniature compression cuff around 1 sciatic nerve	Decreased aldolase activity Decreased lactic dehydrogenase activity
Cat[83]	Surgical preparations Percutaneous bradykinin injections into motion segment	Slowly increasing excitatory discharges Expansion of receptive fields Hyperresponsiveness to subsequent stim

Rat[84]	Mustard oil injection into paraarticular space around C2-C3 joint	Excitatory effects in muscles that were not local, including biphasic response
Cat[85]	T3 and T4 dorsal nerve stim stimulation	Activated cardiac somatosympathetic reflexes
Rat[86]	Dorsal spinal afferent nerve activity	Specific somatosympathetic reflex stimulation

TABLE 4

CLINICAL OUTCOMES INSTRUMENTS IN CHIROPRACTIC RESEARCH

Physical examination:
- Neurologic deficits
- Straight leg raising

Functional outcome assessments:
- Oswestry Back Disability Index
- Roland-Morris Low Back Pain Disability Questionnaire
- Neck Disability Index
- Range of motion
- Muscle strength

Patient perception outcome assessments:
- Pain:
  - Visual analog scale [VAS]
  - Verbal rating scale [VRS]
  - Behavioral rating scale [BRS]
  - McGill Pain Questionnaire [MPQ]
  - West Haven-Yale Multidimensional Pain Inventory [WHYMPI]
- Patient satisfaction
- Patient diary/Duration of episode
- Use of medications

General health and psychosocial assessments:
- Health Related Quality of Life
- Medical Outcomes Study Short-Form General Health Survey
- Sickness Impact Profile
- SF-36
- Dartmouth Primary Care Cooperative Information Project [COOP]
- Million Behavioral Health Inventory [MBHI]
- Modified Zung Depression Index

Costs [direct and indirect]
- All visits to provider
- Prescription/nonprescription drugs or supplements
- Laboratory costs
- Diagnostic imaging
- Referral to specialists
- Hospital costs
- Workdays lost by patient
- Retraining for replacement labor
- Caregiver to assist in domestic duties
- Iatrogenic events
- Legal costs/malpractice

TABLE 5

SCORING CRITERIA FOR RANDOMIZED CLINICAL TRIALS[147]

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1. Similarity of baseline characteristics or adjusted effects reported
2. Concealment of treatment allocation
3. Blinding of patients
4. Blinding of provider/attention bias
5. Blinding of assessor/unbiased outcome assessment
6. Dropouts reported and accounted for in analysis
7. Missing data reported and accounted for in analysis
8. Intention-to-treat analysis/balanced cointervention

1.0 point awarded for YES rating
0.5 point awarded for PARTIAL rating
0.0 point awarded for NO rating

Quality score is calculated by dividing point total by 8 and multiplying the result by 100 to create a 100-point scale.

TABLE 6

CCGPP EVIDENCE RATINGS FOR LOW-BACK PAIN INTERVENTIONS: SUMMARY OF CONCLUSIONS[161]

TOPIC	OF EVIDENCE[a]	STRENGTH
Acute LBP [<6 wk duration]:		
Manipulation	A	
Exercise	I	
Specific exercise	C	
Subacute LBP [6-12 wk duration]:		
Manipulation	A	
Assurance/advice to stay in activities of daily living		B
Customizable exercise programs	B	
Intensive training for severe pain	C	
Chronic LBP [>12 wk duration]:		
Manipulation	A	
Exercise	A	
Assurance/advice to stay in activities of daily living		B
Postsurgical rehabilitation:		
Exercise	C	
Sciatica/radicular/radiating leg pain:		
Manipulation	C	
Assurance/advice to stay in activities of daily living		B

Conclusions exclude patients with red flag findings [contraindications to manipulation].

[a]Grades:

A: Good evidence from relevant studies
B: Fair evidence from relevant studies
C: Limited evidence from studies/reviews
I: No recommendations made because of insufficient or nonrelevant evidence.

TABLE 7

SPINAL MANIPULATION AND CHRONIC BACK PAIN: WEAKNESSES OF SEVERAL RECENT SYSTEMATIC LITERATURE REVIEWS

Assendelft et al:[164]

1. Comparative side effects and relative safety issues are not addressed.
2. There is a mix of clinical judgment without foundation in evidence reviewed.
3. There are inadmissable criteria of quality.
4. The findings are in conflict with those of several national guidelines.[5-11]
5. Meta-analyses themselves are subject to bias and omissions.
6. There are contradictions in design when comparisons are made to sham treatments, general practitioners, analgesics, back school, exercise, physical therapy, and treatments considered to be inferior or harmful.
7. There are contradictions in evaluating clinical and statistical significance.
8. Data are not shown in areas of interest.
9. Fastidious treatments are not the same as complete clinical interventions.
10. There is a lack of long-term followup.

Cherkin et al:[165]

1. There is a failure to resolve conflicting reviews.
2. Exclusions of previous studies are difficult to rationalize.
3. Studies of questionable quality are included.

Ernst and Canter:[166]

1. There is a systematic bias in the current review.

2. The averaging of disparate methodologies and conclusions is arbitrary.
3. There are biases and omissions in other systematic reviews and meta-analyses cited.
4. Comparative side effects and relative safety issues are not addressed.
5. There are flaws in studies in which previous systematic reviews are based.

TABLE 8

SUMMARY OF LEADING OUTCOMES STUDIES INVOLVING SPINAL MANIPULATION FOR MANAGING INFANTILE COLIC

AUTHOR	DESIGN	#S	AGE	INTERVENT	OUTCOMES	RESULT
Wiberg[299]	RCT	25	2-10 wk	SMT F	Crying [hrs]	70% drop, 5 days
		20		Dimethicone		20% drop, 5 days
Olafsdottir[300]	RCT	32	3-9 wk	SMT F	Symptom scale	Improvement 70%
		24		Held 10 min		Improvement 60%
Mercer[301]	RCT	15	0-8 wk	SMT	Parent diary	93% resolved, 2 wk
		15		Detuned ultrasound		
Klougart[302]	PC	316	2-16 wk	SMT F	Crying [hrs]	75% drop, 14 days

Leach[303]	Case	2	6-9 wk	SMT I	Crying [hrs}	50% drop after 1-4x
Pluhar[304]	Case	1	12 wk	[HVLA and I]	Symptom Remission	Resolved
Van Loon[305]	Case	1	12 wk	SMT [Diversified Webster]	Symptom Remission	Resolved

PC = Prospective cohort
HVLA=High velocity low-amplitude
F = Spinal manipulation applied with light fingertip pressure
I = Instrument-assisted [Activator or PulStar FRAS Sense Technology, Inc.]
x = Number of treatments

TABLE 9

SUMMARY OF LEADING OUTCOMES STUDIES INVOLVING SPINAL MANIPULATION FOR MANAGING NOCTURNAL ENURESIS

AUTHOR	DESIGN	#SUBJECTS	AGE	INTERVENTION	OUTCOMES	RESULT

Reed[307]	RCT	31	5-13 yr	SMT	Wet nights/2 wk	16% <baseline	
		15		Sham	0% < baseline		
LeBouef[308]	Cohort	171	4-15 yr	SMT	Wet nights/wk	75% no response	
Blomerth[309]	Case	1	8 yr	SMT	Symptom Remission	Resolved	
Gemmell[310]	Case	1	14 yr	SMT T	Dry/damp/wet	Trend to dryness	

P = Spinal manipulation, Palmer Package Adjusting Technique[311]
T = Spinal manipulation, Toggle Recoil
Sham = Activator at nontension setting

TABLE 10

SUMMARY OF LEADING OUTCOMES STUDIES INVOLVING SPINAL MANIPULATION FOR MANAGING ASTHMA

AUTHOR	DESIGN	#S	AGE	INTERVEN	OUTCOME	RESULT
Balon[316]	RCT	38	7-16 yr	SMT D + S	PEF	Small rise
		42		Sham	FEV	No change
					QOL	Improved
Guiney[317]	RCT	140	5-17 yr	OMT	PEF	Significant rise
				Sham touch		
Nilsson[318]	RCT	31	18-44 yr	SMT Dr	Lung function	Unchanged
				Sham	Symptoms	Improved
					Hyperreactivity	Improved
Ali[113]	RCT	150		C	AQ	SMT decreased
				C	SF-36	SMT decreased
				h	DASS	SMT decreased
				w	Cortisol	SMT decreased
					IgA	SMT increased
Bronfort[319]	Pilot RCT	22	6-17yr	SMT	PEF	N.S. change
		12		Sham	FEV	N.S. change
					QOL	Significant rise
					Severity	Significant drop
					Symptoms	No change
Nilsson[320]	RC	79	2-63 yr	SMT	Symptoms	Resolved
Brocken'r[321]	Crossover	10	>18yr		Thoracic exclus	Significantly reduced
					Sham	No change

Jamison[322]	Cohort	15	8-45 yr	SMT,Mob,Exer	Medication use Reduced		
				Spirometry	No change		
Peet[323]	Cohort	8	4-12 yr	SMT [CBP]	Medication use Reduced		
				PEF	Reduced		
Lines[324]	Case series	3	2-30 yr	Chiro	Symptoms Resolved		
				Medication use	Reduced		
Garde[325]	Case	1	6 yr	SMT	Inhaler use	Ceased	
Hunt[326]	Case	1	4 yr	SMT I	Symptoms	Resolved	
Killinger[327]	Case	1	18 yr	SMT [Palmer UC]	Health status	Improved	
Peet[328]	Case	1	8 yr	SMT	Medication use Ceased		

OMT = Osteopathic Manipulative technique
D = Spinal manipulation, Diversified
S = Soft tissue techniques
Dr = Spinal manipulation with drop table
I = Instrument assisted
PEF = Peak expiratory flow
FEV = Forced expiratory volume
QOL = Pediatric Quality of Life Questionnaire
CBP = Chiropractic Biophysics
UC = Upper cervical
Mob = Mobilization
Exer = Exercise
C = Treatment at centers
c = Nontreatment at centers
h = Nontreatment at home
w = Nonsymptomatic patients at home
AQ = Asthma questionnaire
DASS = Depression and anxiety stress scale
PC = Retrospective case series
N.S. = Not significant

TABLE 11

SUMMARY OF LEADING OUTCOMES STUDIES INVOLVING SPINAL MANIPULATION FOR MANAGING DYSMENORRHEA/PREMENSTRUAL SYNDROME

AUTHOR	DESIGN	#S	AGE	INTERVENT	OUTCOMES	RESULT
Hondras[123]	RCT	138	18-45 yr	SMT Side post	Visual analog	Both groups decreased
				Sham side post	PGE_2	Both groups decreased
Thomason[127]	RCT Pilot	8	17-35 yr	SMT HVLA	Symptoms	Improved
				Sham I		No change
				No treatment		No change

Kokjohn[122]	RCT Pilot	45	20-49 yr	SMT Side post	Visual analog	Decrease in SMT group
				Sham side post	PGE_2	Decrease in SMT group
Snyder[331]	RCS	26		SMT Toftness	MDQ	Improvement
Walsh[332]	Crossover	25	20-47 yr	HVLA soft tiss	Menstrual dist	Decrease in SMT group
				Sham I		
Wittler[333]	Case series	11	23-42 yr	HVLA Gonstead	Symptom	Improvements in all
Stude[334]	Case	1	35 yr	HVLA side post	Symptom	Improvement

HVLA = High velocity low-amplitude
RCS = Randomized comparison study

TABLE 12

SUMMARY OF LEADING OUTCOMES STUDIES INVOLVING SPINAL MANIPULATION FOR MANAGING OTITIS MEDIA

AUTHOR	DESIGN	#S	AGE	INTERVENT	OUTCOMES	RESULT
Mills[339]	RCT	57	6 mo-	RC	AOM	episodes Reduced
			6 yr	RC + OMT	Surgeries	Reduced
Sawyer[340]	RCT Pilot	22	6 mo-6 yr	SMT	Otoscopy Tympanometry Diaries	Feasibile
Froehle[341]	Case series	46	≤5 yr	SMT A SOT AK	Parental decis	93% ep improved
Fallon	Case series	332[342] 401[343]	≤5 yr	RF D,G SMT STE	Otoscopy Tympanometry	Resolved Resolved
Fysh[344]	Case series	5	1-5	SMT [HVLA]	Otoscopy	Resolved
Phillips[345]	Case	1	23 mo	SMT A	Ear drainage, Pain	Reduced
Peet[346]	Case	1	5 yr	SMT {CBP]	Clinical obs	Resolved
Thomas[347]	Case	1	1 yr	SMT	Clinical obs	Resolved

RC = Regular care
OMT = Osteopathic manipulative therapy
SMT = Spinal manipulative therapy
HVLA= High velocity, low-amplitude
A = Activator
CBP = Chiropractic Biophysics
SOT = Sacro-occipital technique [occasionally]
AK = Applied kinesiology [occasionally]
D = Diversified
G = Gonstead
STE = Soft tissue effleurage

RF = 3^o rotation, 5^o lateral flexion
ep = Episodes

TABLE 13

SUMMARY OF LEADING OUTCOMES STUDIES INVOLVING SPINAL MANIPULATION FOR MANAGING HYPERTENSION

AUTHOR	DESIGN	#S	AGE	INTERVENT	OUTCOMES	RESULT
Goertz[137]	RCT	140	25-60yr	SMT/PT/diet	BP	No significant changes
				Diet		
Yates[131]	RCT	21	35-60 yr	SMT I	Sys BP	SMT decrease
				Sham	Dias BP	Sham no change
Bakris[134]	RCT Pilot	26	21-75 yr	SMT [NUCCA]	Sys BP	SMT decrease
				Sham	Dias BP	Sham no change
Plaugher[349]	RCT Pilot	23	24-50 yr	SMT Gonst	BP	Feasibility
				Light massage		
				No treatment		
Morgan[350]	Crossover	29	48-50 yr	OMT, soft tiss	BP	No significant change
Wagnon[133]	Crossover	18	20-50 yr	SMT Gonst	BP	No significant change
					Serum aldost	Significant decrease
McKnight[132]	Cohort	75	20-35 yr	SMT	Sys BP	Significant drop 14/53
				No treatment	Dias BP	Significant

drop 1/22

Knutson[351]	Nonequivalent comparison	54	20-83	SMT No treatment	Sys BP Dias BP	Significant decrease No change	
Fischera[352]	Nonequivalent comparison	35 NL 22 hypertens		OMT	BP	Greater decrease in hypertensive group	
Goodman[353]	Case series	8		SMT	BP	Decrease in 6/8	
Connelly[354]	Case series	3	41-74 yr	SMT SOT	BP	Decrease in 2/3	
Plaugher[355]	Case	1		SMT Gonst	BP	Decrease	
McGee[356]	Case	1	46 yr	SMT HVLA	BP	Decrease	

OMT = Osteopathic manipulative treatment
PT = Adjunctive physical therapy techniques
Gonst = Gonstead chiropractic technique
SOT = Sacro Occipital Technique
NUCCA = National Upper Cervical Chiropractic Adjustment
Sys = Systolic blood pressure
Dias = Diastolic blood pressure
NL = Normal blood pressure

TABLE 14

SUMMARY OF LEADING OUTCOMES STUDIES INVOLVING SPINAL MANIPULATION AND HEART RATE VARIABILITY

AUTHOR	DESIGN	#S	AGE	INTERVENT	OUTCOMES	RESULT
Budgell[97]	RCT	25	21-40 yr	Cervical SMT Sham	HRV	LF increase No change
Budgell[98]	RCT	28	18-40 yr	Thoracic SMT Sham	HRV	LF increase No change
Welch[99]	Case series	3	44-50 yr	Cervical SMT	HRV	LF/HF

decrease (p) increase (s)			47-55 yr	Thoracic SMT		LF/HF
Budgell[369]	Case	1	23 yr	Cervical SMT	HRV	Lost trigeminal pulse Bradycardia remains

LF = Low frequency, power analysis
HF = High frequency, power analysis
(p) = Parasympathetic increase
(s) = Sympathetic increase

TABLE 15

SELECTED NONMUSCULOSKELEAL CONDITIONS RESPONDING TO

SPINAL MANIPULATION OBSERVED IN CASE STUDIES

Condition	Reference
Irritable bowel syndrome	371
Chronic constipation	372
Multiple sclerosis	373
Bell's Palsy	374
Hyperactivity	375
Epilepsy	376
Autism	377
Recovery of visual field loss	378
Temporomandibular joint dysfunction	379

TABLE 16

PROBABILITY OF STROKE OR SERIOUS ADVERSE EVENTS FOLLOWING CERVICAL MANIPULATION

SOURCE	METHOD	RISK
Dvorak[389]	Survey of 203 members of Swiss Society of Manual Medicine [all non-chiropractors]	1 serious complicaton/400,000
Patijn[390]	Review of computerized registration system in Holland	1 complication/518,000
Haldeman[391]	Extensive literature review to formulate practice guidelines	1-2 strokes/1,000,000
Jaskoviak[392]	Clinical files of National College	0 complication/5,000,000 15 year period
Henderson/ Cassidy[393]	Canadian Memorial Chiropractic College Clinic	0 complication/5,000,000 9 year period
Hurwitz[266]	RAND cervical study literature review	0.64 serious complication/1,000,000 0.27 death/1,000,000
Carey[394]	Claim review: Canada's largest malpractice insurance company	1 CVA/3,000,000 0 deaths 5 year period
NCMIC[395]	Claim review: principal chiropractic mal-practice insurance company within U.S.	1 CVA/2,000,000 3 year period
Haldeman[396]	Claim review: Canada's largest malpractice insurance company	0.17 CVA/1,000,000 10 year period

Thiel[397]	U.K. survey of 28,807 treatment consultations	No adverse event

TABLE 17

RISKS IN PERSPECTIVE:
COMPARISON OF DEATH RATES ATTRIBUTED TO VARIOUS CAUSES

RISK	FREQUENCY [PER MILLION]
Neurological complications from cervical manipulation	0.3[266]
Spinal surgery	700[398]
Total hip replacement	4900-15,300[399]
Appendectomies	13,500[400]
Nuclear bone scan	333[401]
Medication errors, outpatient	7633[402]
GI bleeding due to NSAID use	400[403]
Smoking: 20 cigarettes per day	5000[404]
Drinking: 1 bottle of wine per day	75[404]

Canoeing	10[404]
Motorcycling	20,000[404]
Automobile driving [United Kingdom]	169[404]
Soccer, football	39[404]

TABLE 18

RATES OF STROKE COMPARED TO INCIDENCE OF ARTERIAL DISSECTIONS

ATTRIBUTED CAUSE	**RATE [PER MILLION]**
Spontaneous, hospital-based[414]	10-15
Spontaneous, community-based[415,416]	25-30
Cervical manipulation[389]	25
Cervical manipulation[390]	10-20*
Cervical manipulation[392]	0
Cervical manipulation[266]	6.4*
Cervical manipulation[394]	1.7*

*Corrected to represent the average incidence per patient, assuming the average number of manipulations
per patient to equal 10, as reported in the literature.[417]

TABLE 19A

SELECTED ACTIVITIES SUSPECTED OF DISRUPTING CEREBRAL CIRCULATION[405]

Angiography
Bleeding nose
Axial traction
Calisthenics
Cervical extension for xrays or CTS
Cervical rotation while backing up a car
Coughing
Dental procedure
Football
Gymnastics
Hanging out washing
Overhead work
Roller coaster
Telephone call
Traction and short wave diathermy
Trampoline
Watching aircraft
Yawning

_____

_____

TABLE 19B

NONMANIPULATIVE MANEUVERS ASSOCIATED WITH CVAS[418]

Childbirth
By surgeon or anethetist during surgery
Calisthenics
Yoga
Overhead work
Neck extension during radiography
Neck extension for a bleeding nose
Turning the head while driving a vehicle
Archery
Wrestling
Emergency resuscitation
Star gazing
Sleeping position
Swimming
Rap dancing
Fitness exercise
Beauty parlor stroke
Tai Chi

TABLE 20

WORKERS' COMPENSATION BENEFITS IN GEORGIA[469]
Total Weekly Benefits

Claim	YEAR			Group
	2001	2002	2003	2004
A. M.D	$115,590,118	$ 98,419,180	$71,025,150	$18,786,118
Pharmacy	22,426,219	16,292,692	13,310,026	2,228,745
B. P.T.	24,696,617	22,731,637	15,669,193	4,087,587
C. D.C.	850,247	641,805	581,687	184,654
C/A (%)	0.7	0.7	0.8	1.0
C/B (%)	3.4	2.8	3.7	4.5

FIGURE 1

THE HIERARCHY OF CLINICAL EVIDENCE[15]

FIGURE 2

EXTERNAL LINK ANIMAL MODEL FOR SUBLUXATION[35,75]

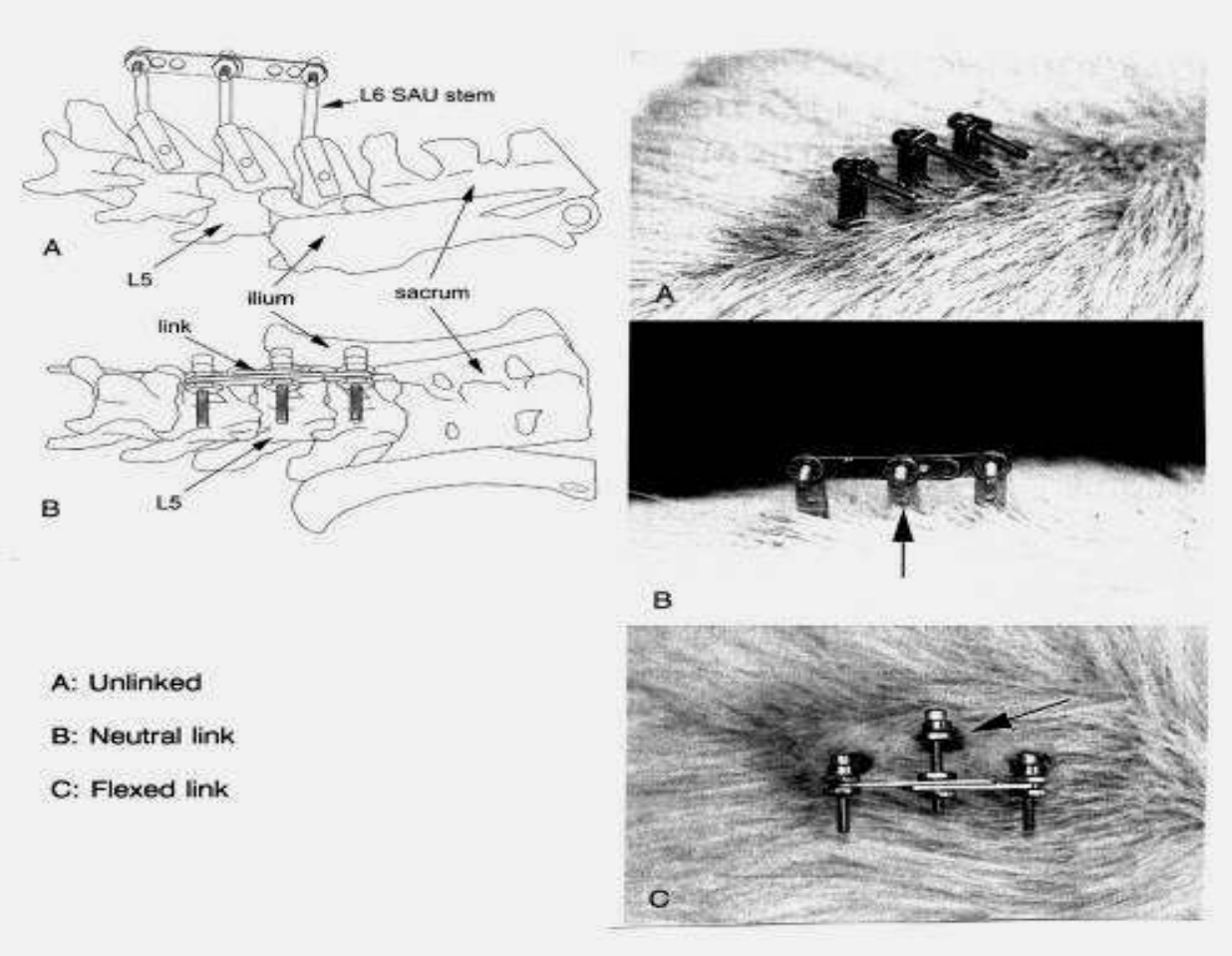


FIGURE 3

INTERACTION OF STRESS WITH VARIOUS BODY SYSTEMS[104]

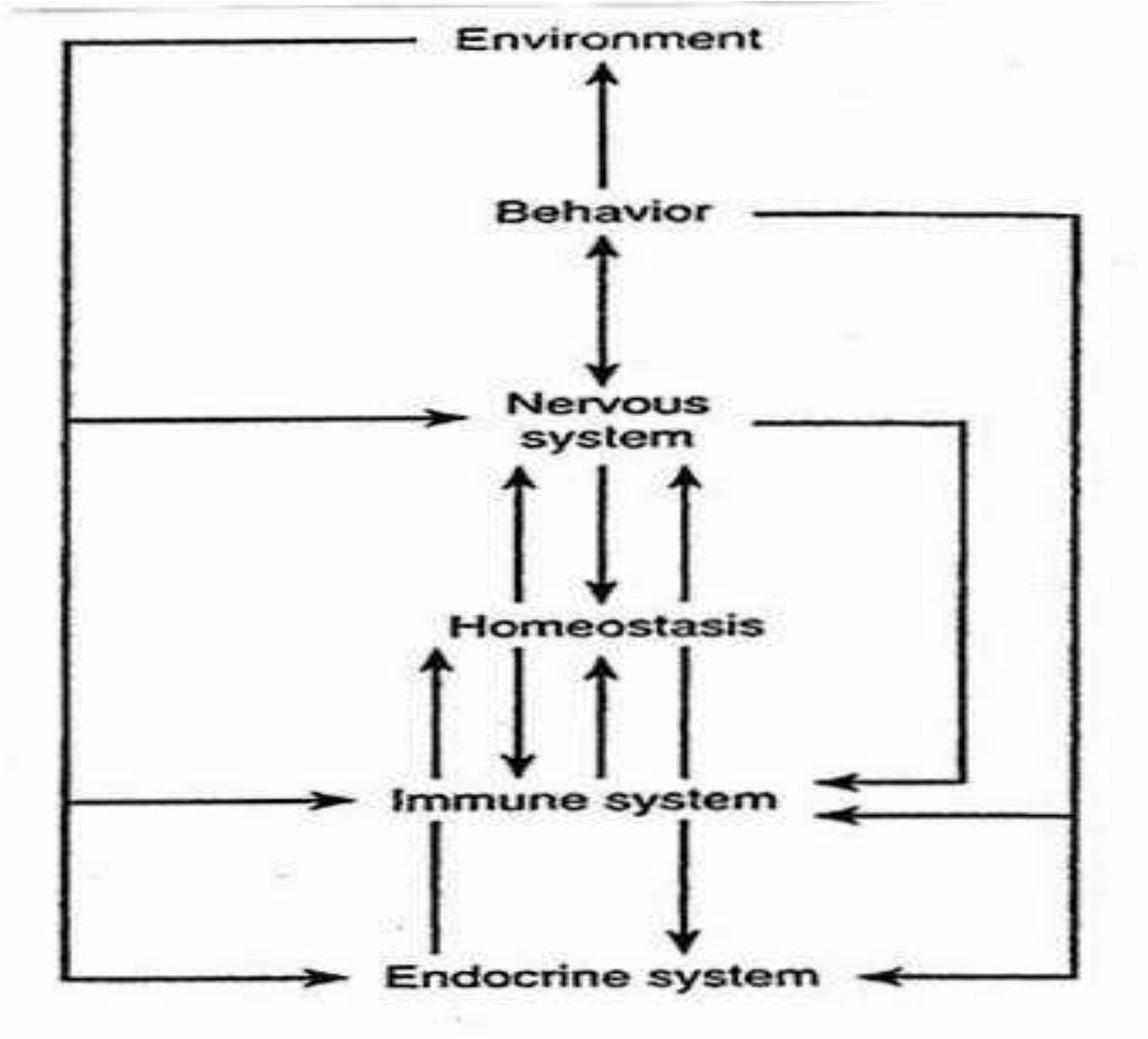


FIGURE 4

PSYCHONEUROENDOCRINE STRESS RESPONSES

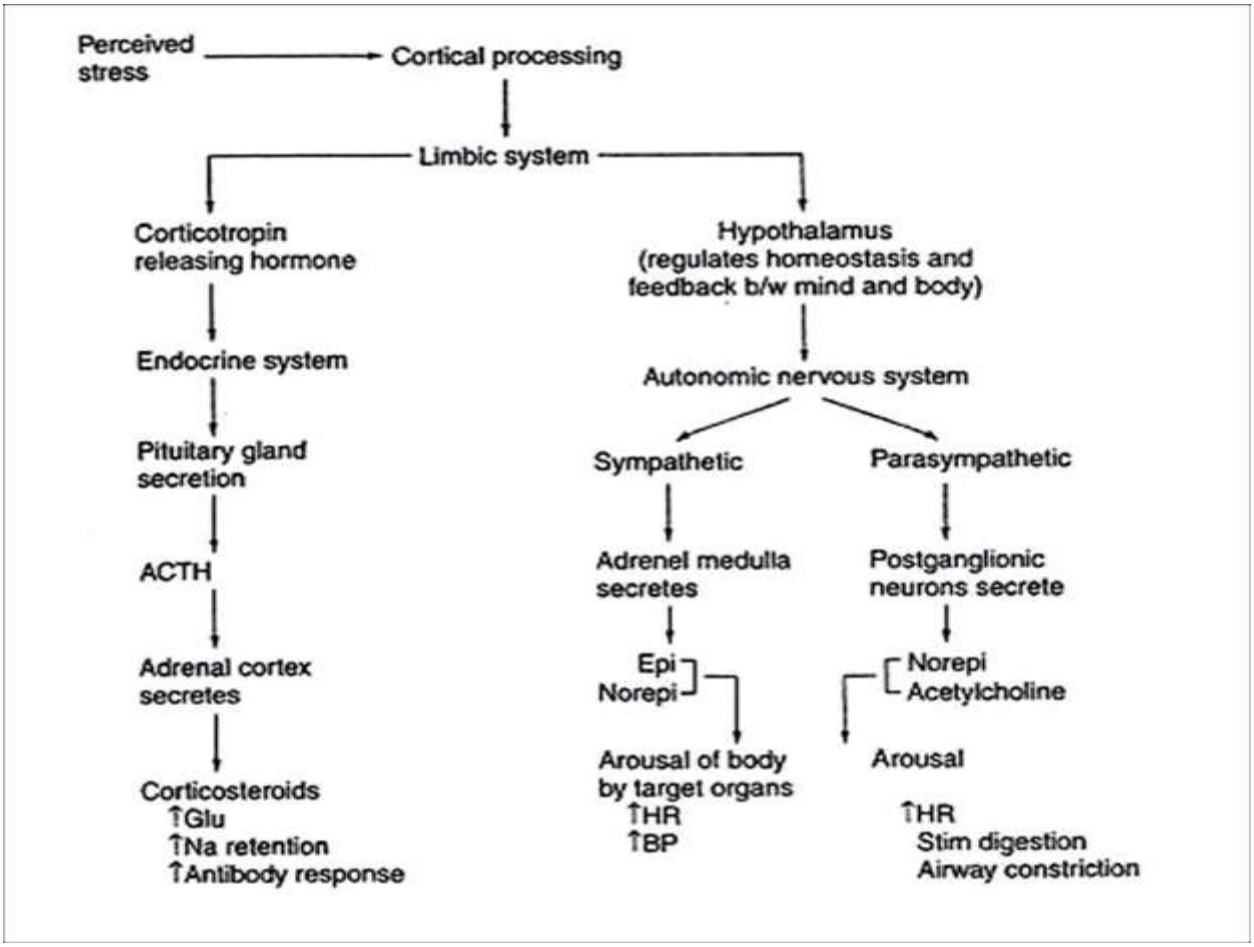


FIGURE 5

CHEMICAL EVENTS FOLLOWING CELL INJURY[139]

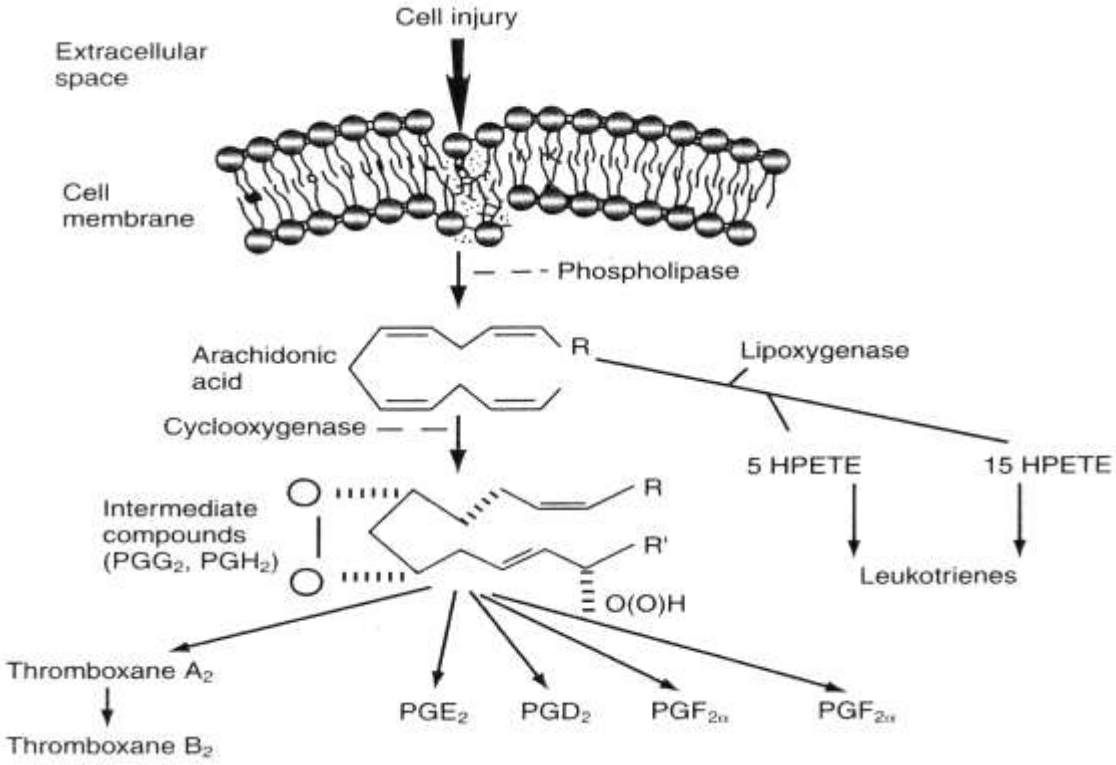

Cell injury
Extracellular space
Cell membrane
Phospholipase
Arachidonic acid
R
Lipoxygenase
Cyclooxygenase
5 HPETE
15 HPETE
Intermediate compounds (PGG_2, PGH_2)
R
R'
O(O)H
Leukotrienes
Thromboxane A_2
Thromboxane B_2
PGE_2
PGD_2
$PGF_{2\alpha}$
$PGF_{2\alpha}$

FIGURE 6

PATIENTS WITH LBP TREATED BY MEDICAL AND CHIROPRACTIC PHYSICIANS: PAIN DAY RECALL AT 36-MONTH FOLLOW-UP: CUMULATIVE PROBABILITIES[170]

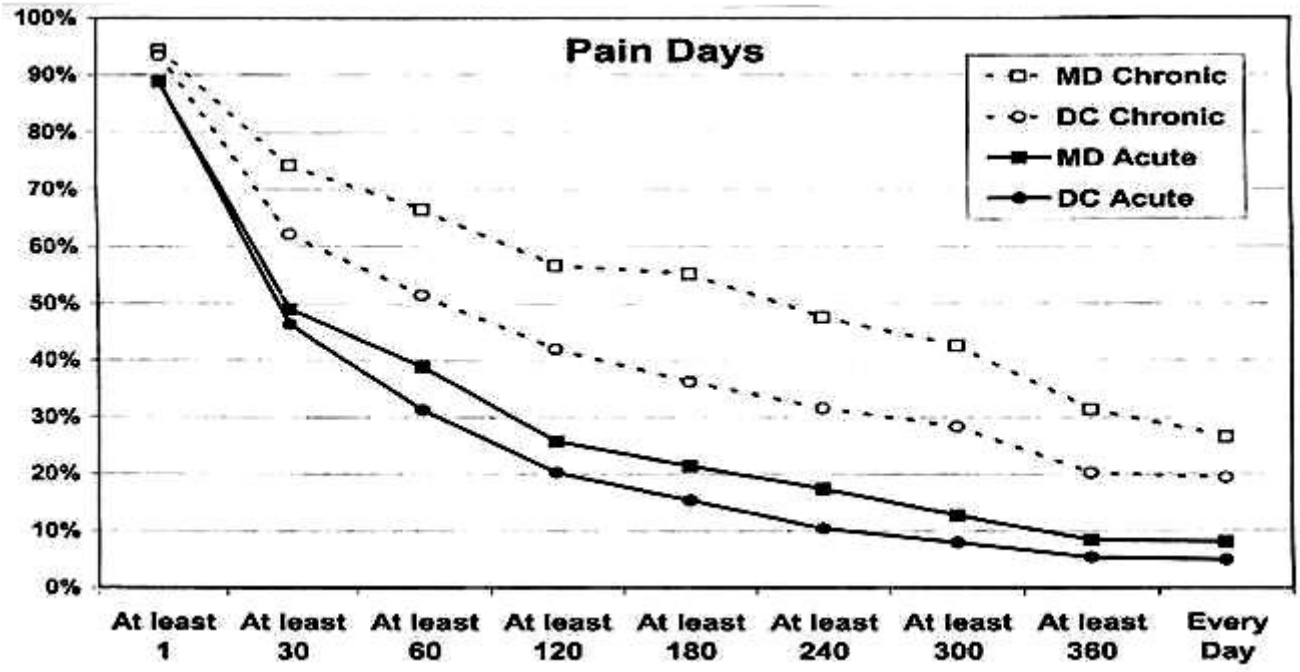
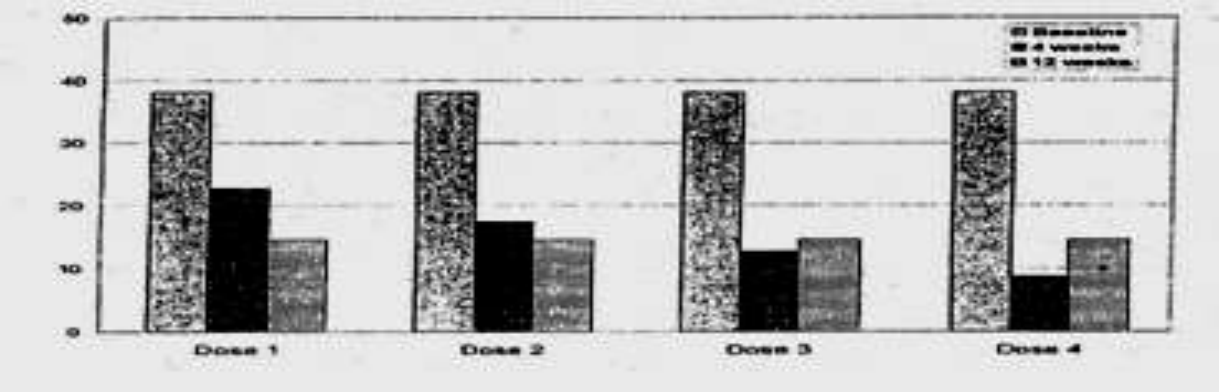


FIGURE 7

DOSE-RESPONSE CHARACTERISTICS OF SMT IN PATIENTS WITH CHRONIC LBP: PAIN INTENSITY AND DISABILITY[173]

Pain Intensity:



Disability:

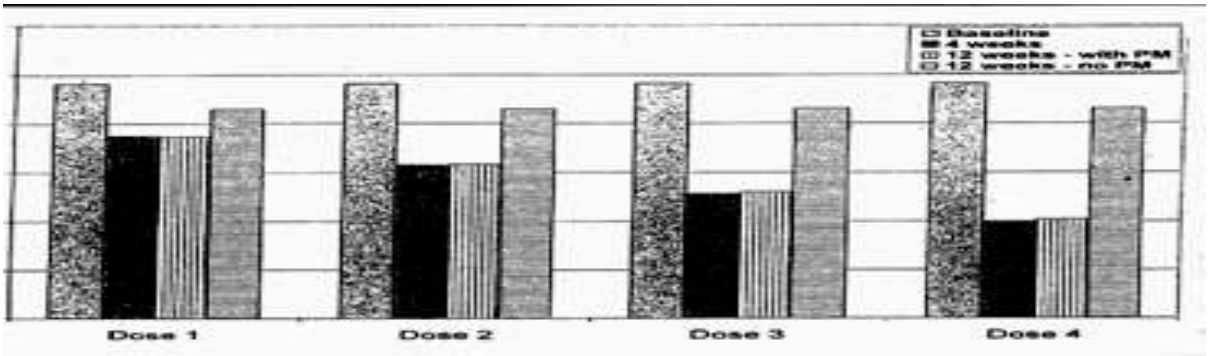


FIGURE 8

OUTCOMES OF TENSION-TYPE HEADACHE PATIENTS IN CLINICAL TRIAL: SPINAL MANIPULATION VS AMITRIPTYLINE[186]

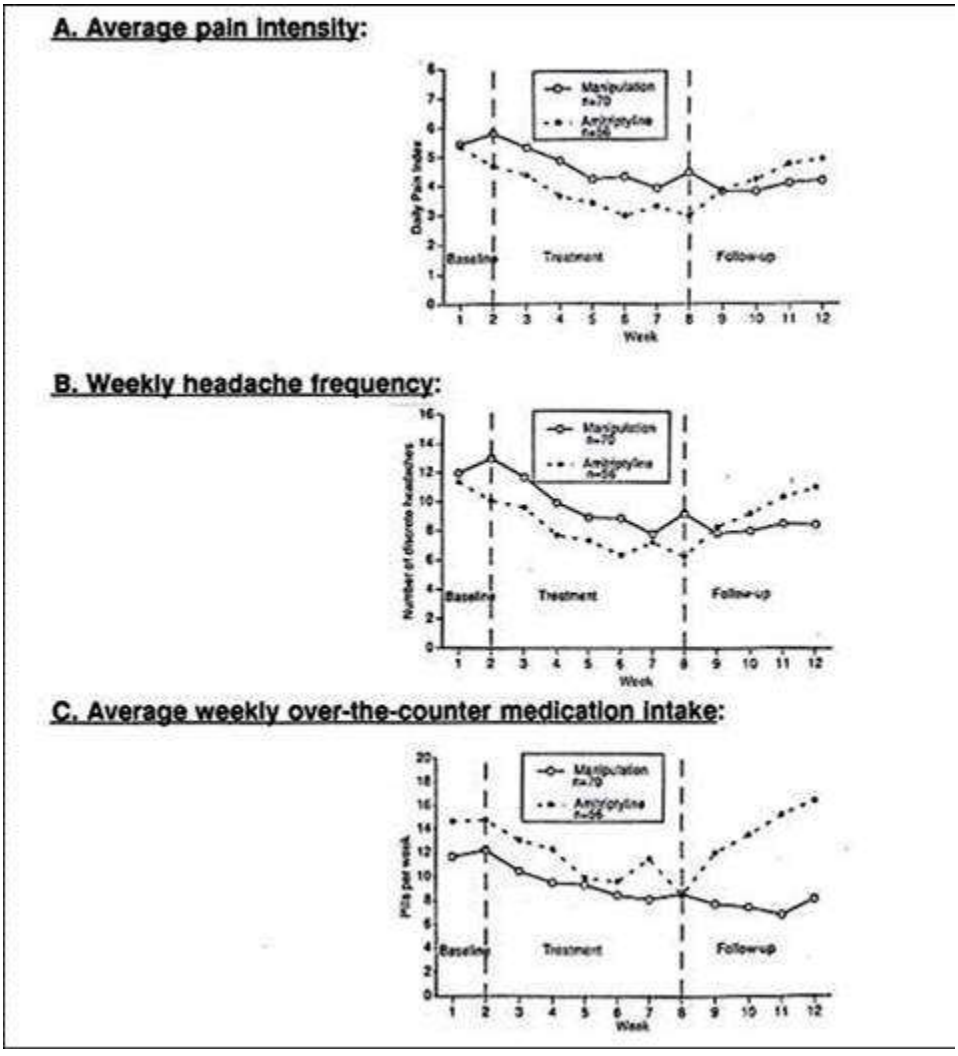


FIGURE 9

CONNECTIVE TISSUE BRIDGE BETWEEN RECTUS CAPITUS POSTERIOR MINOR MUSCLE AND SPINAL DURA[272]

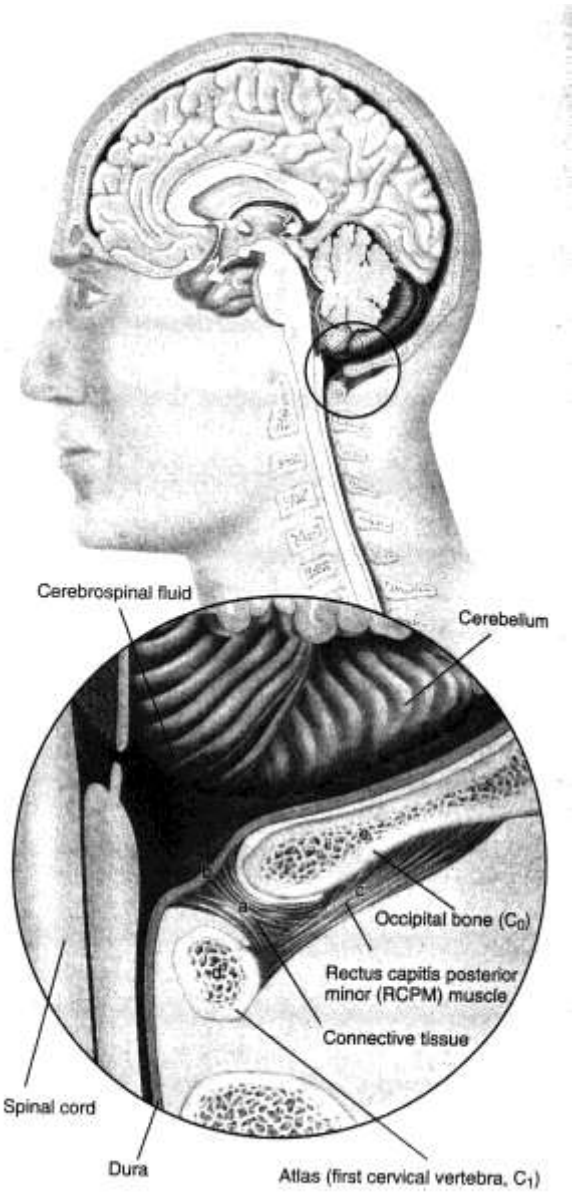


FIGURE 10

RESPONSES OF COLIC TO SPINAL MANIPULATION OR THE APPLICATION OF A SURFACTANT[299]

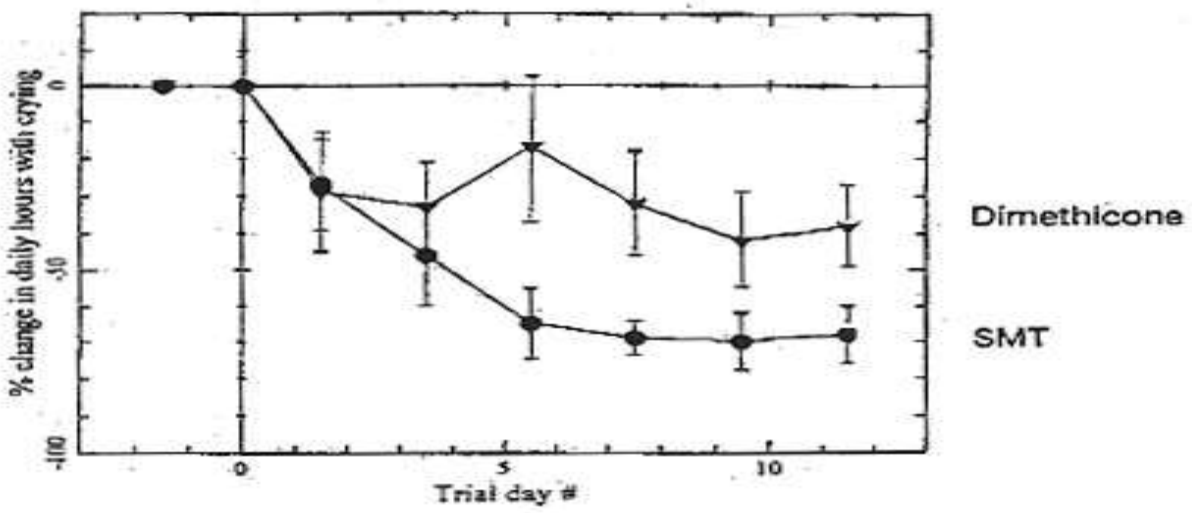


FIGURE 11

THE VERTEBRAL ARTERY BETWEEN THE ATLAS AND AXIS VERTEBRAE[60]

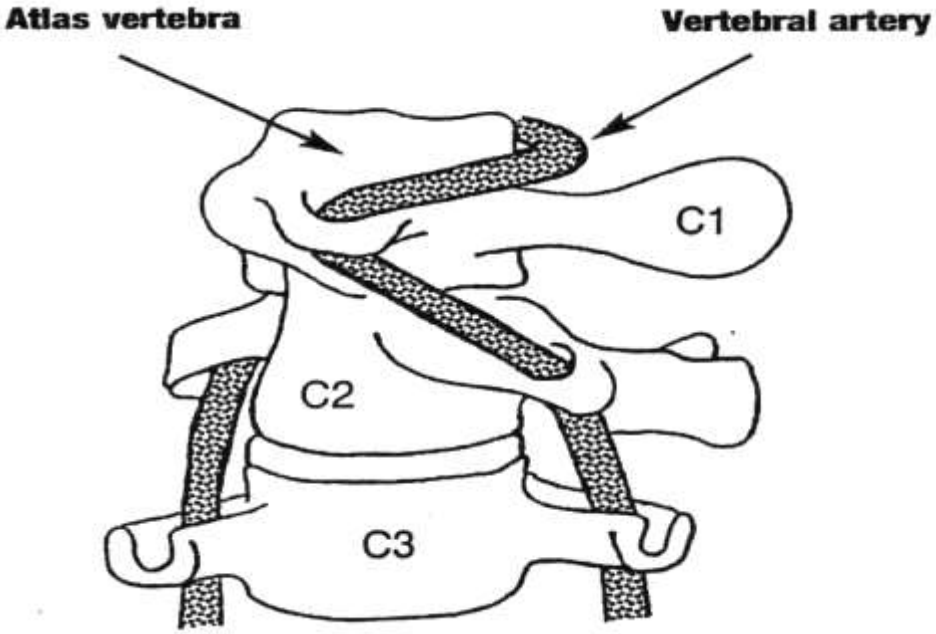

Atlas vertebra
Vertebral artery
C1
C2
C3

FIGURE 12

CROSS-SECTION REVEALING THE LAYERS OF THE CERVICAL ARTERIES[413]

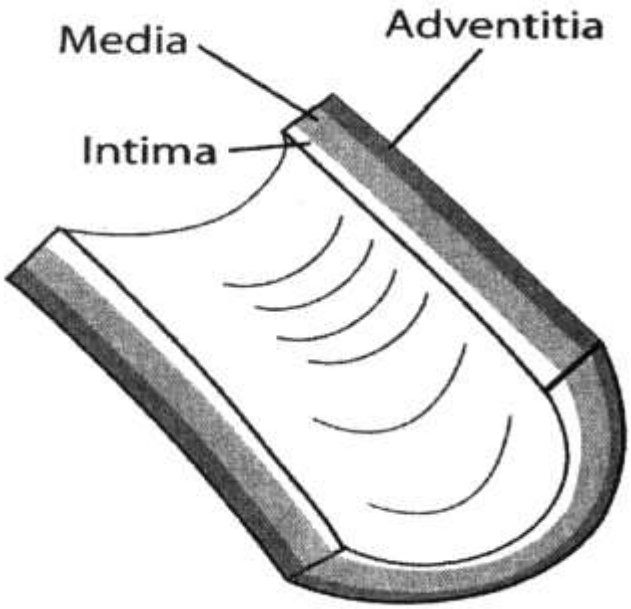
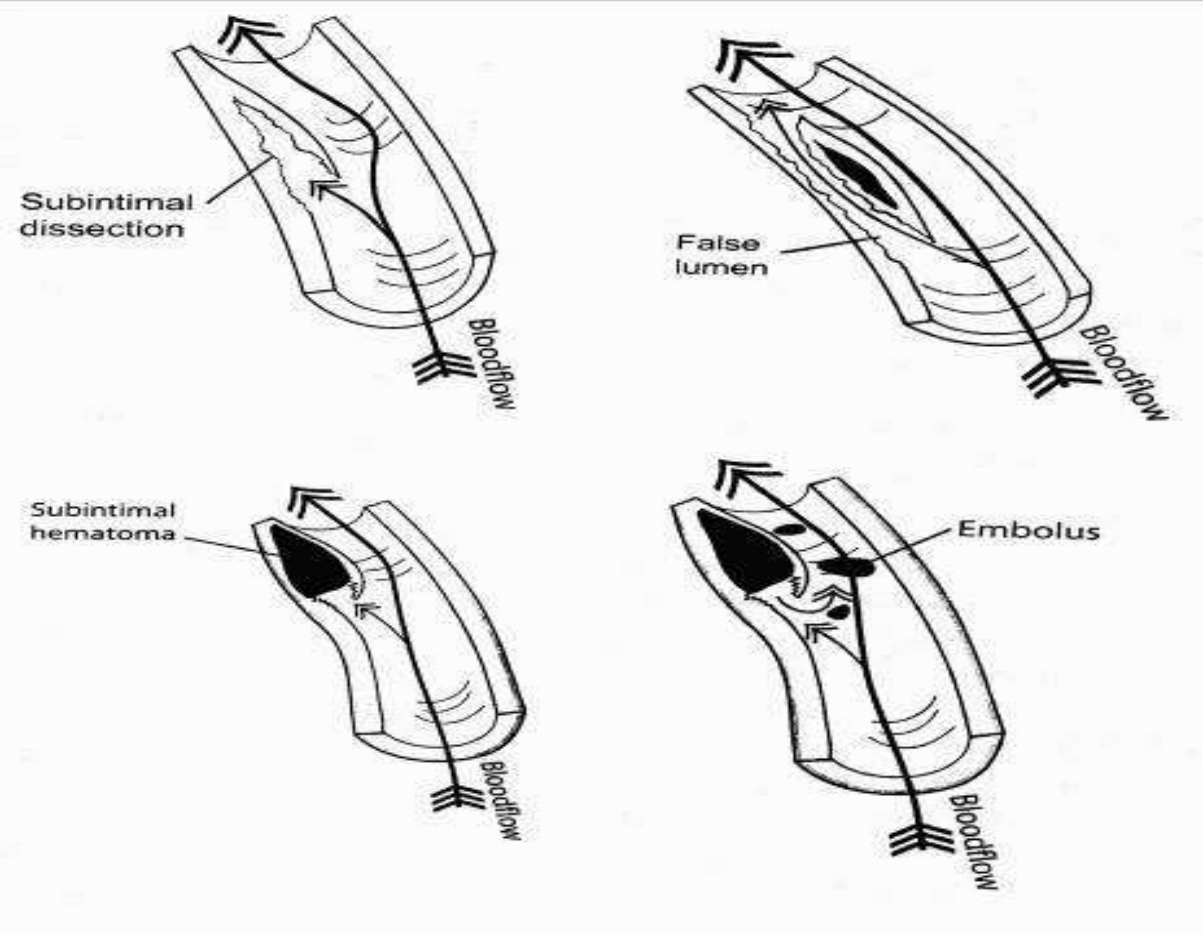


FIGURE 13

DISSECTIONS OF THE CERVICAL ARTERIES[413]



A. INTIMAL TEAR **B. DOUBLE (FALSE) LUMEN**

C. THROMBUS FORMATION **D. DETACHMENT OF EMBOLI**

FIGURE 14

PREVENTIVE SPINAL MANIPULATIVE THERAPY[176]