



META-ANALYSIS AND MANIPULATION: INTERDISCIPLINARY DEBATE

Efficacy of manipulation in low back pain treatment: The validity of meta-analysis conclusions

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Abstract A recent review has concluded that: "Initial studies have found massage to be effective for persistent back pain. Spinal manipulation has small clinical benefits that are equivalent to those of other commonly used therapies. The effectiveness of acupuncture remains unclear. All of these treatments seem to be relatively safe. Preliminary evidence suggests that massage, but not acupuncture or spinal manipulation, may reduce the costs of care after an initial course of therapy" (Cherkin et al., *Ann. Int. Med.* 138(11) (2003) 898). This review was based on a meta-analysis comparing the value of manipulation with massage therapy and acupuncture that concluded that: "There is no evidence that spinal manipulative therapy is superior to other standard treatments for patients with acute or chronic low back pain" (Assendelft et al., *Ann. Int. Med.* 138(11) (2003) 871). A number of opinions were sought as to the validity of these conclusions, and a commentary was offered by Professor Edzard Ernst on these opinions.

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Introduction

Two papers, published in the same issue of *Annals of Internal Medicine* (Assendelft et al., 2003; Cherkin et al., 2003) bring into question the usefulness, compared with other modalities, of manipulation, now widely used in physical therapy as well as, as has always been the case, in chiropractic and osteopathic treatment of many low back pain conditions.

Is this an accurate representation of clinical reality?

What do practitioners using, or defending the usefulness of manipulation in treating back pain have to say about these studies?

Jan Dommerholt, PT, MPS, who specializes in pain and rehabilitation medicine. At the International Myofascial Pain Academy, Bethesda, Maryland, has offered the following considered response to these papers:

To determine the effectiveness of a particular technique or treatment approach, researchers and clinicians have several options. As Moore et al. (1995) have outlined, there is a hierarchy of evidence-based practice ranging from randomized clinical trials (RCTs) to clinical expertise.

Grade 1 evidence involves "strong evidence from at least one systematic review of multiple

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well-designed randomized controlled trials”, whereas grade 5 evidence follows the “opinions of respected authorities, based on clinical evidence, descriptive studies or reports of expert committees”.

Although RCTs are widely used and commonly accepted as “hard evidence”, they may not necessarily be the only or even preferred methodology to evaluate the efficacy or effectiveness of clinical modalities (Gatchel and McGeary, 2002; Moore and Petty, 2001). There are just too many relevant variables in clinical practice, which determine the effectiveness of modalities. These variables include the expertise, training, clinical background, and experience of the practitioner on the one hand, and the pathology, age, gender, fitness level, and other personal characteristics of the patient on the other hand. They may also include such issues as the impact of the patient’s treatment confidence and expectation, fear-avoidance and self-efficacy, interpersonal and psychosocial issues, and socioeconomic and medico-legal factors, among others (Bandura et al., 1987; Goldstein et al., 2002; Mayer et al., 2003; McCracken et al., 1999; Vlaeyen and Crombez, 1999).

Few, if any modalities or treatment approaches currently used by healthcare practitioners have passed the rigor of RCTs. For example, according to RCT-based clinical practice guidelines for shoulder pain only the administration of ultrasound provides clinical benefit with proven efficacy (Philadelphia Panel, 2001) clinicians who have treated patients with varying degrees of shoulder pain would seriously question any guidelines that eliminate soft tissue and joint mobilizations, patient education, neurodynamic maneuvers, posture training, and strengthening and flexibility exercises. In addition, the pain sciences have revealed that there are many mechanisms of pain generation, such as peripheral and central sensitization, expansion of receptive fields, activation of glia cells, gene expression, etc. (Gifford, 2000; Mense, 1993; Watkins et al., 2001; Woolf and Decosterd, 1999; Yaksh et al., 1999). It is hard to believe that ultrasound would be the only modality suited to alter glia activation in chronic shoulder pain. In other words, while there is value to conducting RCTs, the conclusions of many meta-analyses indicate little beyond the observation that there are few well-designed RCT studies with adequate control of dependent and independent variables, sufficient numbers of subjects, adequate follow-up, etc.

Assendelft and colleagues completed an extensive RCT-based meta-analysis comparing the effectiveness of spinal manipulation to sham therapy,

general practitioner care, analgesics, physical therapy and exercises, back school, and a group of ineffective interventions, such as traction, a corset, bed rest, etc. (Assendelft et al., 2003). They concluded that “there is no evidence that spinal manipulative therapy is superior to other standard treatments for patients with acute or chronic low back pain”. In an accompanying review article, Cherkin and colleagues agreed that, “spinal manipulation has small clinical benefits that are equivalent to those of other commonly used therapies” (Cherkin et al., 2003). Both studies indicate that spinal manipulation is superior to sham treatment and at least equivalent to other established interventions. Given the many variables in patient care, it should come as no surprise that spinal manipulation or for that matter, any other single therapy, is not the silver bullet for clinical practice. There is no reason to remove spinal manipulation from the box of clinical tricks. There is growing evidence that spinal manipulation has distinct neurophysiological effects and may be useful in counteracting central pain mechanisms (Pickar, 2002).

Cherkin et al. (2003) acknowledged that in the real world, clinicians use “collections of various interventions that are often tailored to the needs of individual patients and that reflect the specific practitioner’s training and preferences”. The key to effective patient care lies in the unique combination of therapeutic interventions.

While spinal manipulation may not be superior to other approaches, the practice of acupuncture was described as “questionable” (Cherkin et al., 2003). The question emerges whether RTCs of the effectiveness of single interventions are useful. Is it possible to control all necessary variables in an effort to test one intervention? Should the conclusions of this study be used to steer patients away from acupuncture? Or should we recognize that it may not yet be possible to evaluate the effectiveness of acupuncture given the small number of well-designed studies, the wide variety in acupuncture approaches, the limited knowledge of acupuncture, etc? The theoretical framework of acupuncture is the subject of many studies and reviews (NIH Consensus Conference, 1998; Hui et al., 2000; Langevin et al., 2001a,b; Takeshige et al., 1992). At this point of time, we may have to rely on grade 5 evidence of “opinions of respected authorities, based on clinical evidence, descriptive studies or reports of expert committees”. The bad news is that so often, studies like this can be used by third parties to deny payment, referrals, etc. even though the limitations of RCTs are well recognized (Gatchel and McGeary, 2002).

On a side note, it seems odd to compare spinal manipulation to physical therapy without defining physical therapy in more detail. The authors seem to equate physical therapy with nothing but exercise. Yet, spinal manipulation is a common modality in physical therapy practice throughout the world (Paris, 2000).

Douglas Lewis ND, head of the Physical Medicine Department at Bastyr University, Seattle, has responded as follows:

On June 3, 2003 the *Annals of Internal Medicine* published the results of a meta-analysis of studies examining the effectiveness of acupuncture, massage, and spinal manipulation for the treatment of back pain. The authors of the study (Cherkin et al., 2003) conclude that massage is effective for the treatment of persistent back pain, spinal manipulation has small benefits comparable to other commonly used therapies, and that the effectiveness of acupuncture remains unclear.

Following publication of the report, one of the authors, Shekelle, was quoted in the popular press as saying

“Our study should temper some of this enthusiasm (for spinal manipulation) by demonstrating that, on average, there is no difference in outcomes for patients treated with spinal manipulative therapy compared to other recommended care, like analgesics, exercises, or physical therapy.”

This review and the subsequent comments regarding it demonstrate once and for all that the debate as to the value of spinal manipulation and other alternative therapies used for the treatment of back pain rages on.

Let us explore some of the implications of the conclusions drawn by the authors. The “spin” put on the results of studies such as this is that if a therapy is not found to be effective, it must follow that it is ineffective. Cherkin et al., state in their review that spinal manipulation was found to have “small clinical benefits that are equivalent to those of other commonly used therapies”. Later, Shekelle was quoted as saying “there is no evidence that spinal manipulative therapy is superior to other standard treatments for patients with acute or chronic low back pain” with the implication that there is therefore no benefit to be gained from manipulation (i.e. the implication being that if spinal manipulative therapy is not more effective than other common therapies it is automatically ineffective).

Tonelli and Callahan (2001) take this sort of argument apart. They state that “some individuals in any large clinical trial may have causally benefited from an intervention that failed to

demonstrate efficacy across the population as a whole.”

That is to say, effectiveness may not be demonstrated for a large group, but is not disproven for the individual.

If it is found that two different interventions are equivalent in outcome, isn't it appropriate to select the safest of them? Wolfe et al. (1999) indicate that an estimated 103,000 Americans are hospitalized each year for serious gastrointestinal complications from taking NSAID drugs and that about 16,500 patients die each year from NSAID-related problems. Are not the risks of NSAID great enough that it makes sense to use an equivalent, safer therapy such as spinal manipulation whenever possible? Andersson et al. (1999), conclude in a study of osteopathic manipulative therapy for back pain that

“Osteopathic manual care and standard medical care have similar clinical results in patients with subacute low back pain. However, the use of medication is greater with standard care.”

The authors also found that patients used less physical therapy. Again, the choice of therapy is clear if it avoids the use of potentially risky medications.

One common argument against spinal manipulation is that this care is more expensive than “standard care”. It stands to reason that if a patient is prescribed medication for a complaint, they would not go back to the doctor unless they need a new prescription. They also would not go back to the doctor who is only able to offer drugs that are not effective for their particular problem. Care is cheap if no one is using it.

Return-to-work is also used as a measure of the effectiveness of a therapy. However, it is rarely reported whether patients return to work in pain or not. If it is discovered that patients with sub-acute, non-surgical back pain all return to work after approximately the same amount of time off, is it possible that they returned to work because their sick-time ran out?

Our current research paradigm requires reductionist thinking. What single or small number of variables can we consider to play a role in a certain expected outcome? What we discover depends on what outcome we are measuring. The really important question is “Are we measuring the appropriate outcome?”

This brings us back to Tonelli and Callahan. It may be that alternative medicine cannot be evidence-based if the epistemology of evidence-based-medicine does not fit that of alternative medicine.

It is in fact likely that there is no one-size-fits-all therapy for back pain. Evidence-based medicine such as that applied by Cherkin et al. may give us a general guideline as to the efficacy of an intervention, but clinical evidence must lead us to apply individualized interventions to individual patients.

In my own practice I find that a multi-factorial approach is superior to a single intervention for most patients. Some patients respond well to soft tissue manipulation and stretching. Others do well with spinal and/or other joint manipulation. Most patients do better with both therapies applied in concert.

Any practitioner who has seen a patient arrive at his or her office in acute pain, and seen that pain disappear rapidly following joint manipulation, will certainly continue to manipulate. Any reasonable physician who does not see his or her patients improve with an offered therapy will change that therapy in search of one that fits the needs of that particular patient. The study of medicine may be the study of the average effect for a group, but the practice of medicine must be the application to an individual.

Chiropractor **Craig Liebenson** DC, a leading authority in spinal rehabilitation ([Liebenson, 1996](#)) has offered the following perspective.

A recent meta-analysis of research up to January 2000 review by Assendelft et al. shows that spinal manipulative therapy has efficacy and is effective. The question remaining is how does it compare to other effective treatments?

Compared to sham treatments or ineffective treatments – such as bed rest – spinal manipulation has demonstrated its efficacy. It is certainly an effective treatment and this is not due merely to a placebo effect.

However, there are numerous other effective treatments which patients can choose from. These include general practitioner care, analgesics, physical therapy and exercise. Future studies will want to compare the satisfaction, costs, frequency and duration of these various treatments to determine which is more effective. Additionally, these treatments should be compared to patient sub-groups thought to be ideal for each different treatment approach.

Unfortunately, most research on the effectiveness of different treatments treats back pain patients as an homogenous group ([Van Tulder et al., 1997](#)). [Laboeuf-Yde et al. \(1997\)](#) points out that low back patients are a heterogenous group. If research assumes a large patient population is homogenous then it would fail to show statistical clinical effectiveness for specific interventions beneficial for a certain smaller sub-group. The

result is that a promising treatment would be erroneously assumed to be ineffective.

Work at the University of Pittsburgh has shown that sub-classification of the “non-specific” group is possible with an evaluation consisting of a thorough history, disability questionnaires, and examination utilizing a battery of simple, reliable tests including sacroiliac and McKenzie ([Erhard and Delitto, 1994](#); [Fritz and George, 2003](#); [Fritz et al., 2000](#)). Treatment which is matched to the appropriate sub-classification is superior to unmatched treatments ([Erhard and Delitto, 1994](#)).

A recent randomized, clinical trial (RCT) not reviewed by Assendelft shows that treatment driven by sub-classification is superior to the “generic” treatment recommended by the Agency for Health Care Policy and Research (AHCPR) for low back pain ([Fritz and George, 2003](#)). Outcomes included reduced disability and accelerated return to work. Treatment classifications included manipulation/mobilization of lumbar or sacro-iliac joints, centralization (McKenzie) with flexion/extension, stabilization, and traction for nerve root syndromes not exhibiting a centralization phenomena.

[Flynn et al. \(2002\)](#) demonstrated that low back pain patients who were most likely to respond favourably to spinal manipulation could be identified by the presence of the following five predictors:

- (1) Segmental dysfunction/pain upon springing palpation over lumbar facets
- (2) Acute onset of pain < 16 days.
- (3) No pain distal to the knee.
- (4) Hip internal rotation limited.
- (5) Low fear avoidance beliefs score.

These five factors comprise what is called a “clinical prediction rule” because their presence increases the likelihood of success with the studied treatment modality. The presence of four of five of these variables (positive likelihood ratio = 24.38) increased the probability of success with manipulation from 45% to 95%.

In summary, spinal manipulation:

- is more effective than traditional treatments such as bed rest which have been exposed as ineffective or even harmful.
- has proven that it is more than a placebo treatment.
- when compared with a variety of other valid treatment options (such as acupuncture) has not shown that it is superior.

In fact, no treatment has shown that it is more than moderately successful in treating low back pain. Assendelft et al. point out that low back pain

is a very significant disorder in Western society involving as it does work loss and heavy medical expenditures. Prior meta-analysis had concluded that spinal manipulation was more effective than shown in this study, primarily due to its being compared to ineffective approaches such as bed rest, diathermy, traction and corsets. When compared to more effective treatments, manipulation was not shown to be superior.

Assendelft et al. concluded that future studies of spinal manipulation should concentrate on cost-effectiveness. The Fritz and Flynn studies (2000, 2002, 2003) indirectly do that by showing that those patients most likely to respond to manipulation can be identified by a classification analysis. This work was not available to the Assendelft group and should be considered in any conclusions drawn about the overall effectiveness of spinal manipulation.

Some of the points made by Dommerholt, Lewis and Liebenson are echoed in several shorter responses from other experts:

Zachary Comeaux D.O., of West Virginia College of Osteopathic Medicine, says:

"I think the literature review is short-sighted since the literature regarding manipulation is not yet mature, or reflective of our work. Outcome studies are hung up on the issue of defining a treatment population. There is inconsistency in identifying homogenous populations because of the issue of inter-rater reliability in diagnosing. This is not unique to the field of manual medicine, as orthopedic medicine has a very hard time developing a gold standard for assessing back pain.

This lack of standardization magnifies itself when one realizes the operator dependent variability in treatment, both between and within professional disciplines. The bottom line then is that manipulation for back pain is not universally the same, despite the labelling. I do not have answers to these problems but give them due consideration regularly."

John Hannon D.C. elaborates:

"The problem with spinal manipulation being studied in this way is that it is used for many different purposes. Touch hunger, the yearning for an attentive ear, the quest for a trustworthy somatic guide, all of these cloud the picture of why people seek manipulators. The effective clinician supplies all of these along with healthy doses of charismatic placebo. I doubt that anyone gets a tuberculin skin test or dental work just for the touch, but many people attend manipulators with unstated, and understudied, needs. To scientifically study manipulative efficacy, I feel a new model is needed, before statistical studies are made about outcome. A model which includes the psychosocial dimension is needed. Science, as a tool, requires the control of all but the studied variable.

This kind of control is unlikely for manual medicine in general and spinal manipulation in particular. Perhaps the validation of exam and treatment using inter-examiner reliability studies is still stuck in the doldrums for this reason."

Peter Gibbons D.O., Victoria University, Melbourne, adds:

"There is increasing expression of the view that, while it might be difficult to provide evidence of the efficacy of single interventions, a multi-modal approach to patient care for given conditions is likely to be the way forward. It may also be the case that different types of intervention may be more effective at different stages in the natural history of a complaint. I don't know the answer but perhaps exercise may show better outcomes in prevention of recurrence, rather than acute management for given conditions."

Recent research

A recent trial compared the effects on low back pain of osteopathic manipulative treatment (OMT) with sham treatment and no treatment ([Licciardone et al., 2003](#)).

The results showed that:

- "In comparison with usual care alone, usual care and OMT provided better outcomes in back pain, physical functioning, mental health, use of cotreatments, and satisfaction with back care.
- Usual care and sham manipulation also provided better outcomes in back pain and physical functioning and greater satisfaction than usual care alone.
- Usual care and OMT did not provide significantly better low back outcomes than usual care and sham manipulation."

The evidence supporting use of manipulation remains equivocal, based on this osteopathic study ([Licciardone et al., 2003](#)) involving people with constant or intermittent, non-specific low back pain for at least 3 months. It was found that both osteopathic manipulation techniques [OMT] ("myofascial release, strain-counterstrain, muscle energy, soft tissue, high-velocity-low-amplitude thrusts, and cranial-sacral...aimed at somatic dysfunction in the low back or adjacent areas") and sham manipulation ("range of motion activities, light touch, and simulated OMT techniques [consisting of] manually applied forces of diminished magnitude aimed purposely to avoid treatable areas of somatic dysfunction and to provide minimal likelihood of therapeutic effect") were superior to no treatment.

However the results showed similar benefits for both “real” and “sham” treatment, when used alongside usual care for the treatment of chronic non-specific low back pain. It is therefore unclear whether the benefits of manipulation can be attributed to the techniques used, or whether they are related to other aspects, such as range of motion activities or placebo effects – or whether use of “clinical prediction” methodology might have produced different outcomes?

There is clearly much still to learn about what aspect of manipulation helps back pain!

Conclusions

- People with back pain do not represent a homogenous population (age, gender, etiology of back pain, degree of chronicity, expectations, etc.), making it difficult, if not impossible, to compare like with like when assessing the meaning of different research papers focusing on back pain.
- People performing manipulation have hugely varied levels of skill and training, and use a wide variety of manipulative techniques, even when these are labelled similarly, creating obstacles to comparison of like with like.
- Randomized clinical trials are probably not the ideal tool for measuring methods such as manipulation for the reasons outlined, making a meta-analysis of such trials a less than accurate means of establishing the value of this treatment method.
- When appropriately selected using the “clinical prediction rule” (see discussion relating to Flynn et al., 2002 in Liebenson’s response above), patients show a very high positive response to manipulation (up to 95% success rate).
- Lack of proof of efficacy does not prove a method is ineffective, only that proof is lacking.

Professor Edzard Ernst’s commentaries on some of the responses listed above:

In my view the meta-analysis by Assendelft et al. is authoritative, thoughtful and by far the most definitive piece of evidence about the effectiveness of spinal manipulation (SM) available to date. Of course, it is disappointing that the overall conclusions are not more encouraging. But this could well be due to the lack of a convincing overall effect of SM rather than any bias of the authors. In fact, I know that the team has worked long and hard and comprises all necessary types of expertise to render this meta-analysis as free of bias as

achievable in such meta-analyses. My comments to the above remarks are as follows.

Cherkin’s analysis of SM was based on the Assendelft article, which is why we should probably concentrate on this one only.

Dommerholt repeats the often-voiced argument that the RCT may not be the best methodology to test the effectiveness of SM. We probably all know that RCTs have some limitations. Until someone shows us conclusively a superior (less prone to bias) tool, I would insist that there is presently no better.

He also states that “few if any” conventional therapies have “passed the rigor of the RCT”. This may be so for back pain, but as a general concept this statement could confuse readers. The problem of heterogeneous groups is virtually ubiquitous. This is why randomization is such a clever idea. If done well, it renders both groups in a typical RCT comparable in all measurable and unmeasurable characteristics. When comparing one trial to another, heterogeneity may well be a problem. In meta-analyses, one can do subanalyses (like Assendelft did) to get a handle on it. We also should look at the consistency of effects across studies. If there are “outliers” we might ask “were these patients in any way different?”

In clinical trials one should obviously try to minimize variability, e.g. by choosing only well trained therapists treating to a standardized protocol.

Depending on the research question, one might also conduct a pragmatic study along the principle “do the chiropractors practising in Exeter collectively generate better outcomes than GPs?”

One would then hope that individual differences disappear in the overall average which is the target of such a study. Clinical research often means making compromises and is fraught with challenges, obstacles and problems. The perfect study clearly does not exist. This is why aggregated results from all studies are more meaningful than a single trial.

Liebenson cites two new studies by Flynn et al. (2002) and Fritz and George (2003). Both are important papers which point us into the direction of finding ways of differentiating responders from non-responders of SM. The studies are preliminary by nature and suggest a range of criteria for differentiation. What is needed now is an independent replication of these results. Subsequently we can begin to plan studies to test whether some patients reproducibly respond to SM while others do not or even get worse.

As I have mentioned, these are important lines of investigations. To assume that we already have cracked this tough nut, would be, in my view, counter-productive.

Liebenson also believes that “this work..(i.e. Flynn and Fritz)...should be considered in any conclusions drawn about the overall effectiveness of SM”.

I do not see how this is possible. If we come up with classifications for potential responders today, we cannot easily apply them to trials conducted yesterday. I am afraid that the responder-hypothesis requires prospective testing, and the onus to do this work is on those who adhere to it.

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