LITERATURE SYNTHESIS* - MANIPULATIVE THERAPY OF LOWER EXTREMITY CONDITIONS (DRAFT)

A Systematic Review by the Research Commission of the Council on Chiropractic Guidelines and Practice Parameters

*A literature synthesis is an academically rigorous analysis of all the available scientific literature on a specific topic. Reviewers use internationally accepted tools to rate each article according to specific criteria. These include the type of study (randomized controlled trial, case series, etc), the quality of the study, size of the study and many other factors which influence the credibility and strength of the study's conclusions. Each reviewer independently rates all the available articles, and the ratings are compared among the members of the review team. When there is disagreement among the reviewers regarding the conclusions, a formal consensus process is followed to arrive at an overall conclusion upon which all reviewers can agree. The resulting conclusions do not represent the reviewers' own beliefs but rather what the literature actually supports. A literature synthesis is a starting point. It indicates only what we can conclude with supportable, scientific evidence. Appropriate therapeutic approaches will consider the literature synthesis as well as clinical experience, coupled with patient preferences in determining the most appropriate course of care for a specific patient.

Team Lead
James Brantingham DC, PhD
Director of Research and Associate Professor
Cleveland Chiropractic College Los Angeles (CCCLA)

Team Members
Gary Globe, DC, MBA, PhD
Provost Cleveland Chiropractic College, Los Angeles
Cleveland Chiropractic College, Kansas City and Los Angeles

Henry. Pollard DC, PhD
Director of Research and Associate Professor
Department of Health and Chiropractic,
Macquarie University, NSW 2109, Australia

Marian Hicks, MSLS
Director of the Library and Media Resource Center
Cleveland Chiropractic College Los Angeles

Charmaine Korporaal, MTech:Chiropractic
Head of Department and Research Supervisor,
Department of Chiropractic
Durban University of Technology, Durban, South Africa

Wayne Hoskins, BChSc, MChiro
School of Medicine, University of Melbourne, Parkville, Australia

Table of Contents

Summary of Recommendations

Topic	Conclusion and Strength of Evidence Rating	page
Hip Osteoarthritis	**RATING: C** Limited evidence to support manipulative therapy of the hip combined with multimodal or exercise therapy	**11**
Knee Osteoarthritis	**RATING: B** Manipulative therapy of the knee and/or full kinetic chain combined with multimodal or exercise therapy	**13**
Patellofemoral Pain Syndrome	**RATING: B** Manipulative therapy of the kneww and/or full kinetic chair combined with multimodal or exercise therapy	**14**
Ankle Inversion Sprain	**RATING: B** Manipulative therapy for ankle sprain with multimodal or exercise therapy	**15**
Plantar Fasciitis	**RATING: C** Manipulative therapy for plantar fasciitis with stretch/and or multimodal/ exercise therapy	**17**
Metatarsalgia	**RATING: C** Manipulative therapy for metatarsalgia with and without multimodal therapy	**17**
Hallux Limitus/Rigidus	**RATING: C** Manipulative therapy for hallux limitus/rigidus with multimodal therapy	**18**
Hallux Abductor Valgus (HAV or bunion)	**RATING: I** Manipulative therapy for hallux abductor valgus	**18**

Introduction

In 2006, Hoskins et al published the first extensive, ranked review of chiropractic treatment of lower extremity conditions.[1] Building upon Hoskins et al's efforts and using similar methodology and structure, the present study represents an expanded and updated systematic review. While gratefully acknowledging Hoskins et al for their 2006 review, the conclusions in this manuscript are solely those of the included CCGPP subcommittee authors.[1]

In the Hoskins et al review, "*chiropractic treatment"* was operationally defined as some form, technique or procedure utilizing applied manipulative therapy (manipulation, mobilization, and/or other manual or functional procedures) *with and without* adjunctive treatment. For the purposes of this updated and expanded literature review, "*chiropractic"* has been replaced by the term "*manipulative therapy"* to facilitate inclusion of all literature from accessible peer-reviewed sources.[2] While the public generally associates chiropractic primarily with the treatment of back pain, only a minority of practitioners perceive themselves solely as spine specialists.[3] The data actually demonstrates that most chiropractors, based upon their professional training, routinely diagnose and treat extremity conditions.

It is of great importance to the chiropractic profession to elevate the awareness of the general public, government, third party payors as well as other stakeholders regarding the training and competency of chiropractors to care for extremity conditions. While chiropractors can easily document the use of *manipulative therapy* (with and without adjunctive treatment) for lower extremity neuromusculoskeletal problems and disorders for 100 years, other healthcare providers, such as physical therapists, general and family physicians and acupuncturists are more commonly recognized as able to care for the entire axial and appendicular neuromusculoskeletal system.[1,4,5,6, 7,8,9]

Depending upon the source, extremity problems (upper and lower combined) have been reported to account for up to 20% of all of chiropractic care with lower extremity pain and injury specifically accounting for up to 10% of common chiropractic practice with the majority of practitioners utilizing extremity manipulative therapy based upon location, methodology, training and philosophy.[4,3,10,11,12,13,14,15] This significantly contrasts to treatment of non-musculoskeletal conditions such as chest, abdominal pain and wellness, 5.3, 3.7% and 8.0% respectively.[3, 4]

Actually, extremity treatment is the second most frequently applied procedure within the chiropractic profession with 76.1% reportedly using spinal and extremity procedures as compared to 18.7% who limit their practice to the spine only.[3] Indeed, chiropractic academic curriculums are significantly directed towards neuromusculoskeletal disorders associated with the *full appendicular* (including axial) skeleton, and include training in anatomy, biomechanics, differential diagnosis, radiology, radiographic positioning, orthopedics, sports medicine, first aid, rehabilitation and *extremity diagnosis and treatment*.[1] Certainly, based upon their academic training, the current chiropractic graduate is well qualified to manage peripheral disorders.

Further exemplifying the chiropractic profession's contribution as the forerunner to extremity care, in a recent 2004 trial of high velocity low amplitude axial elongation *thrust* manipulation (*hereafter* HVLA manipulation) of the hip (with associated stretching) conducted to determine efficacy in treatment of hip osteoarthritis (including grade 4 radiographic degeneration with severe pain and stiffness), HVLA manipulative therapy was substantially superior to an evidenced based hip exercise protocol.[16,17]

Notably, *this trial utilized the most common, and possibly oldest chiropractic manipulative procedure employed for hip disorders and osteoarthritis over the last century*, further supporting previous, preliminary studies and reports completed on and before 2004.[18,19,20, 21] Significantly, this trial suggests a possible alternative treatment for (1) those who may not, or should not have surgery, (2) those who may not, or should not chronically use non-steroidal anti-inflammatory drugs (NSAIDS) and (3) those in whom exercise alone is not effective.[22,23,24] [25,26,27,28,29] Although research and publications on manipulative therapy in the treatment of peripheral disorders, such as the one just reviewed, has recently exploded, much more study is required.[1,30, 31,32,33] It is clear that extremity care is not the exclusive domain of any singular healthcare discipline, and in that spirit, the authors encourage chiropractic, physical therapy and medical and other researchers to work alongside as well as collaboratively in the search for improved clinical methods for the treatment of patients with lower extremity conditions.[16,21,34,35]

In the presence of a rapidly expanding number of research studies as well as growing attention on the usefulness, utilization and treatment of peripheral disorders through manipulative therapy management, the authors believed that it would be helpful, in this all inclusive context, to broadly revisit the evidence and review the quantity, quality and types of lower extremity manipulative therapy research conducted and published, and to rank, grade and present the characteristics of such research, thus providing a more general, complete and updated review.[1,36,33]

Methods

In conjunction with the CCCLA librarian and with input from included authors, an expanded update of the Hoskins et. al 2006 review was undertaken with a search of the literature conducted using CINAHL, MEDLINE, MANTIS, Science Direct, and Index to Chiropractic Literature from December 2006 to February 2008.[1] Limits were set to English abstract, and human. Search terms including *chiropractic, osteopathic, orthopedic* or *physical therapies* were searched with MeSH terms for each region. *Manipulation* or *mobilization treatment* for the lower extremity was also searched using MeSH terms. For the hip, this included hip injuries, hip dislocation, and hip joint. For the knee, this included the terms knee dislocation, knee injuries, knee joint, collateral, meniscus, and patellofemoral. For the ankle, this included ankle injuries, tarsal bones, and ankle joint lateral ligament. For the foot: foot bones, foot injuries, foot joint and interphalangeal. And finally for the ankle: ankle injuries, tarsal bones, and ankle joint lateral ligament. In addition to the literature previously reviewed[1] a further 389 citations

were captured from the 4 regions searched: 33 hip, 86 knee, 249 ankle, and 21 foot respectively.

After the abstracts were reviewed, the literature was placed into three broad categories. Category 1 included randomized controlled or clinical trials (RCTs) with manipulative therapy (with and without adjunctive or multimodal therapy such as exercise/rehabilitation, modalities, NSAIDS, and activity modification, etc.).[1] The Category 1 evidence table included; (1) randomized controlled trials (RCT) which indicates these studies were *placebo* controlled; (2) randomized clinical trials (RCT^) which denotes a *comparative* study (*treatment versus treatment; usually with evidence superior to placebo*); (3) controlled or clinical trials (CTs) which are generally *pseudo* or non-randomized (with systematic assignment or purposive allocation) containing a range of controlled variables, peripheral diagnosis, manipulative therapy versus placebo, comparative treatment or both; and (4) studies that are prospective, measurable, and generally include valid and reliable outcome measures with appropriate statistical analyses.

Category 2 included case series (≥ 3 patients per study). For case series, the co-chairs of the CCGPP Scientific Commission developed a checklist modified from other instruments. Category 3 included case studies (≤ 2 patients), but studies <u>*not*</u> included in the previous review. Inclusion criteria required peripheral diagnosis and some variety or mode of manipulative therapy. Articles were excluded when (1) pain was referred from spinal sites (without peripheral diagnosis), (2) there was referral for surgical intervention (unless there was documented *full* postsurgical healing with or without rehabilitation), (3) the condition was not amendable for manipulative therapy (RA, fracture, ligament tear with instability, etc), (4) a red-flag diagnosis was identified or (5) there was a peripheral diagnosis absent a description of management or intervention. In the current review, osteopathic, physical therapy and other medical literature was included, however, review-type articles were excluded. Non-peer-reviewed literature, conference proceedings, grand rounds, and discussion articles with no rendered treatment were also excluded.

Abstraction of data was independently completed by three independent authors using set criteria. Articles were retrieved as hard copy, PDF or electronic format from the Cleveland Chiropractic College Los Angeles library, or from associated library collections. All clinical trials found to be relevant were assessed, reviewed and ranked using a modified Liddle et al adaptation of the Scottish Intercollegiate Guidelines Network or "SIGN" ranking system (instead of the Physiotherapy Evidence Database or "PEDro" scale utilized in the previous review).[37,38, 39,40] General use of SIGN is in conformity to CCGPP systematic reviews. When documenting treatment, standardized terminology was utilized, therefore, the term "manipulative therapy" indicated any the following terms: (1) all types, methods, modes, techniques and procedures of mobilization and manipulation grades I through V (2) all adjustment/adjustive procedures and (3) manual or manipulative therapy procedures.[2,41,42,43]

The SIGN scale, modified Liddle et al revision and limitations of SIGN

One methodological difference between this and the Hoskins et al 2006 review grew out of CCGPP concerns with the disproportionately inflexible weighting structure represented by *singular* SIGN components that makes the application to burgeoning areas of historically, weakly supported research, such as is the case with manual therapy, difficult at best and was believed to potentially and otherwise mask the helpful information that could be yielded through the assessment of this literature base. Current SIGN checklist and component explanations discard older, previously acceptable randomization techniques with any non-computerized randomization completely rejected. The literature supports the appropriateness of the *restricted* use of manual and mechanical randomization methods, particularly in small samples.[44,45,46,47] Additionally, SIGN's over-emphasis and weighting of a few scale components, excluding all other methodological considerations, is inconsistent with other validated, widely accepted systems such as JADAD or PEDro where randomization and intention to treat analyses are considered as *one* of a number of important methodological concerns, *assigning decreased weight, depressing, not rejecting, overall trial quality*.[48,47]

In accordance with these above stated concerns, controlled and clinical trials were ranked using a modified Liddle et al revision of the SIGN scale.[1,37,38,39] While the SIGN RCT checklist rates studies as high quality (+), low quality (-) or neutral (n), the *modified* Liddle et al SIGN scale (see **Table 1** and further discussion below) utilizes (++) for high quality with very low risk of bias (+) for well conducted studies, with low risk of bias or (-) for studies with few, no or inadequately fulfilled or described criteria, with high risk for bias.[37,38]

Table 1. SIGN Rating Scale.

+ +	Applies if all or most criteria from the checklist are fulfilled; where criteria are not fulfilled, the conclusions of the study or review are thought very unlikely to alter.
+	Applies if some of the criteria from the checklist are fulfilled; where criteria are not fulfilled or are not adequately described, the conclusions of the study or review are thought unlikely to alter.
-	Applies if few or no criteria from the checklist are fulfilled; where criteria are not fulfilled or are not adequately described, the conclusions of the study or review are thought likely or very likely to alter.[36,37]

Liddle et al's SIGN revisions have undergone rigorous development and validation procedures, part of a hierarchy of studies widely accepted as reliable.[39,40] Further, Liddle et al's SIGN revisions have been evaluated, adapted and developed by multiple review groups, assessed for methodological rigor, clarity, and practicality in clinical use (principally for diagnosis but utilized in this review to rank trials) with studies repeatedly finding their checklists producing reliable and consistent results.[38,39,40]

Some of the trials cited in this expanded review (principally smaller studies) utilized earlier, non-computerized randomization procedures then in wide use by various

researchers at institutions such as Durban University of Technology in Durban, South Africa and the University of Surrey in Guildford, England where much of the pioneering work in lower extremity manipulation research originated. These randomization procedures were accomplished utilizing equal numbers of obscured and folded sheets of paper (for example 15 or 30 marked A; 15 or 30 marked B) thoroughly mixed assuring discontinuity, placed in and blindly extracted from a container. At each subject randomization time-point, containers were held such that all folded slips were masked and a slip was drawn out randomly allocating treatment. This older procedure, long used in medicine prior to accessible, affordable computerized randomization, remains acceptable for samples of N≤ 60 (n≤ 30 per group).[44,45,46] Consequently this review's use of a modified SIGN ranking means manual and mechanical randomization procedures were given *decreased* methodological weight, indicating lesser quality, but not rejected.[47,48]

Evidence based care, with its *hierarchy of evidence*, notably includes private practice, field, and expert advice and does not posit care rendered only by evidence from RCTs as this has been determined to be neither economically feasible, practical, scientific *or* ethical.[46] With these considerations in mind, this study includes non-randomized, systematically assigned, controlled or clinical trials designated as *CTs* as well as the addition of unlisted or new case series and studies excluded by previous criteria and added in ranked and updated case series and studies sections. Additionally, studies using *systematic assignment* (with *less* bias), no longer considered validly randomized, have been, after consideration, included in this review because, as some of the first and foundational studies ever performed, they frequently utilized or contain significant innovative methodological controls, concepts and insights. Such studies, evaluated by the present authors as certainly equal to retrospective case series, have been previously treated as if they constitute no evidence at all, discarded as worthless; and incorrectly excluded from the "evidence based" hierarchy.[37, 44,45,46,47,48,49]

Arguably CTs could be placed in Category 2, but increased controls within these CTs often markedly exceed typical case series. In comparing against many peer reviewed published RCTs, with high levels of inadequate, erroneous and/or incorrect report of per protocol or intention to treat analysis as well as disagreement, lack of consensus or standards regarding blinding and blind assessment, there is a sufficient justification and rational for inclusion of these RCTs and CTs.[1,16,32,50,51,52,53,54,55,56,57,58,59,60,61]

Intention to Treat Analysis (ITA) can be a useful tool in interpreting study data. For example when data from subjects who drop out of a study secondary to adverse effects is excluded, this certainly constitutes a potential bias in interpreting findings that would benefit from the addition of ITA. But the retrospective requirement of ITA levied on all previous studies, including some well done smaller trials, can, at times result in completely discounting evidence that should be considered on some level of the hierarchical ladder.[46,56,57] Furthermore, in many studies with ITA, particularly in systematic reviews of ITA, it is evident that many authors have significant and serious objections to *ITA* being a sole, or *the* sole arbiter of a valid or legitimate trial (SIGN simply *rejects* studies that do not use ITA).[62,63,64,65] Hollis et al point out that 52% of

medical trials fail, do a poor or an inadequate job with ITA.[62] In a recent systematic review of 249 trials, Gravel et al pointed out that, even now, randomization was used only 77% of the time, ITA only 23% of the time, with ITA in general done poorly, incorrectly, or unclearly explained.[63] Porta et al cautions that ITA or Per Protocol analysis (PP) is so often flawed, and flawed to such an extent, that it is wrong to base conclusions of a controlled trial on single report of either ITA or the PP approach alone.[64] Baron et al found that, out of 54 trials, full ITA analysis was done correctly in these studies only 7.4% of the time.[65] For this reason, *like randomization*, it is of utmost importance to utilize a ranking methodology that balances rigor with reason so as to yield the best evidence possible from the existing literature. Therefore, in this review, the absence of ITA results in a *lower* study rating. Furthermore, if essentially all subjects that began the trial complete the trial, ITA was rated as adequate.[46,62,63,64,65]

The initial step of utilizing the modified Liddle et al SIGN to rank study methodology was followed by a synthesis and considered judgment whereby the authors scored the evidence with Grades of "A, B, C and I" as outlined in the *Handbook for the Preparation of Explicit Evidence-Based Clinical Practice Guidelines* [66] **(see Table 2).** The "*considered judgment on quality of evidence" was applied to all* reviewed materials, including case series and studies from the previous review, and assessed per the grading recommendations as listed in Table 2 below.[1,38,66]

Table 2: Grading of recommendations

GRADE A: Good evidence from relevant studies.

- Results from studies with appropriate designs of sufficient strength to answer the questions addressed.
- The results are both clinically important and consistent with minor exceptions.
- The results are free of any significant doubts about generalizability, bias, and flaws in research design.
- Studies with negative results have sufficiently large sample sizes to have adequate statistical power.

GRADE B: Fair evidence from relevant studies.

- Studies of appropriate designs of sufficient strength, but inconsistencies among results, or minor doubts about generalizability, bias, and research design flaws, or adequacy of sample size.
- Evidence consists solely of results from weaker designs, but results confirmed in separate studies.

GRADE C: Limited evidence from studies/reviews.

- Studies of appropriate, but substantial uncertainty due to design flaws, or adequacy of sample size.
- Limited number of studies or because of weak design for answering the question addressed.

GRADE I: No recommendation can be made because of insufficient or non-relevant evidence.

There is no evidence that directly pertains to the addressed question because either the studies have not been performed or published, or are non-relevant.

Results

Of the total 389 citations, 39 were determined to be relevant (and thus supplementary to the clinical or controlled trials previously found by Hoskins et al), Of these 39 studies, 8 pertained to conditions affecting the knee, 1 regarding the hip, 7 regarding the ankle (with new information regarding 1 trial previously excluded as non-randomized) and 2 regarding the foot. These studies, randomized controlled and/or clinical trials (a few by systematic assignment or purposive allocation) were assessed. The case series and studies previously incorporated in 2006 have not been cited in this investigation, therefore readers are referred to that review; however, 13 case series and studies excluded and/or not previously reported in a single source are included; 3 regarding the hip, 2 regarding the knee, 2 regarding the ankle, and 6 regarding the foot**.**

Evidence:

There is a level of **C** or limited evidence for manipulative therapy combined with multimodal or exercise therapy of the hip, for hip osteoarthritis.[1,16, 21, 67, 68,69] There is a level of **B** or fair evidence for manipulative therapy of the knee and/or full kinetic chain combined with multimodal or exercise therapy for knee osteoarthritis.[1,28, 29, 54,70,71,72,73] There is a level of **B** or fair evidence for manipulative therapy of the knee and/or full kinetic chain combined with multimodal or exercise therapy for Patellofemoral Pain Syndrome.[1,53,74,75,76,77,78,79] There is a level of **B** or fair evidence for manipulative therapy of the ankle and/or foot combined with multimodal or exercise therapy for Ankle Inversion Sprain.[1,32,50,51,55,80, 81, 82, 83,84, 85,86] There is a level of **C** or limited evidence for manipulative therapy of the ankle and/or foot combined with multimodal or exercise therapy for Plantar Fasciitis.[1,52,86,87,88] There is a level of **C** or limited evidence for manipulative therapy of the ankle and/or foot combined with multimodal or exercise therapy for Metatarsalgia.[1,86,89,90,91] There is a level of **C** or limited evidence for manipulative therapy of the ankle and/or foot combined with multimodal or exercise therapy for Hallux Limitus/Rigidus.[1,50,92,93,94] There is a level of **I** or insufficient evidence for manipulative therapy of the ankle and/or foot combined with multimodal or exercise therapy for Hallux Abducto Valgus/Bunion **(see Table 3).**[1,95] Tables 4-7 **(see Tables 4-7)** summarize additional case series and studies and will be commented upon in the discussion section.

Table 3. Evidence table of manipulative therapy for lower extremity disorders*

Author	Study type	Condition	Participants	Intervention/ Control	Follow-up	Results/ outcomes		Grade (below)	Rating
Hip									
Hoeksma et al[16]	RCT^ (see § below)	Hip Osteo-arthritis	N=109 Age 60-85 Mean age 71.5	HVLA axial elongation hip manipulation with stretch vs exercise	9 txs/ 5 weeks. 5 weeks 17 weeks 29 weeks FU	Significant in favor of man therapy: primary, 2nd outcome measures (Likert scale): self report % improvement, and Harris Hip Score, VAS, ROM No serious but minor ↑ side effects: 3 left man group, 2 exercise		Adequate power, Adequate blinding Int to tx covered	++
Brantingham et al[21]	CT ¥ Systematic Assignment randomized 1st patient (then A,B etc) Blind assessor/1 unblinded	Hip Osteo-arthritis	N=8 Ave Age 69.8	HLVA axial elongation and other manipulations and mobiliz. of hip joint vs Placebo	6 txs/ 3 weeks 7 weeks 1 week FU 2 withdrew (N=10)	Significant effect size for man ther: WOMAC, NRS vs Placebo ROM, Fabere unchanged in tx group No side effects. 1 exclud got PT. 1 sham left - pain to high		Cohens *d* Large effect size changes	+
Level of evidence for Manipulative therapy for hip Osteoarthritis		Average no. of txs: 7.5 over 3-5 weeks Range 6 to 9 (2 trials)				1 high quality, 1 low quality trial		**Grade of Evidence: C** (Man ther of the hip combined with multimodal or exercise therapy)	

Knee									
Deyle et al[54]	RCT	Knee Osteoarthritis	N=83 Mean Age 61	Manipulative therapy of knee and full kinetic chain SI – foot vs Placebo=non therapeutic Ultrasound Knee man: mob knee ↑ flex, ext, patellar mob (gradually up to 4++ or thrust)	8 txs/4 weeks 4 weeks 8 weeks 1 year	Significant in favor of man therapy: at 4 & 8 weeks. 8 weeks WOMAC ↓ 55%, ↓ time 6 min walk. 1 year FU - WOMAC, walk significant. Arthroplasty 20% placebo, 5% in tx group.		Adequate power Int to tx covered	++
Deyle [70]	RCT^	Knee Osteoarthritis	N= 134 Mean Age 63	Man therapy of knee and full kinetic chain - SI to foot vs Home Exercise Knee man: mob knee ↑ flex, ext, patellar mob (gradually up to 4++ or thrust)	8 txs/ 4 weeks 4 weeks 8 weeks 1 year	Significant in favor of man therapy at: 4, 8 weeks with WOMAC 52% to exercise 26%. 1 year FU both significantly improved but: man ↑ satisfaction, ↓ meds		Adequate power Int to tx well covered	++
Tucker et al[71]	RCT^ Assessor not blind	Knee Osteoarthritis	N=63 Mean Age 59.3	CMT to the Knee (HVLA) vs Meloxicam 1/x day for 3 weeks. Knee man: long axis, A-P, P-A and patellar mob NSAID previously superior to placebo	8 txs/ 3 weeks	No difference between txs. Significant improvement both: NRS, VAS, PSFS. 3 left trial: NSAID side effects: nausea, diarrhea, allergic		No patients left man ther group	+
Moss et al[29]	RCT Allocated to 3 txs Assessor, patients blind	Knee Osteoarthritis	N=38 Adults ≥ 40	Supine A-P mobilization of Tibia on Femur Within subjects repeated measures vs placebo (holding position) vs no contact	1 tx Immediate post intervention No drops outs	Significant ↓ in pain (= ↑ in Algometry) and ↑ speed in 'up and go' (from chair).		Adequate power Adequate blinding Int to Tx adequate	+

Bennell et al[28]	RCT Double blind	Knee Osteoarthritis	N=140 Age 68.6	PT program: knee taping, exercise, ST, *thoracic spine mobilization* vs Placebo	PT and Placebo tx: <u>8 txs</u> 1x/week for 4 weeks then 1x/2 wks for 8 wks (8 txs). 13 dropped out PT (2 side effects others various reasons) 2 in placebo	No significant difference between groups Significant outcome for PT at 24 weeks for VAS pain, global improvement (2 areas) out of 12 assessments (VAS pain and activity, WOMAC, KPS, SF-36, *AQoL*, quad strength, step test).		Power adequate, In to tx good, Poor design and internal validity: *<u>Thoracic spine manipulation?</u>* Non standard No man therapy for knee/LE	**+**
Level of evidence for Manipulative therapy for Knee Osteoarthritis		Average no. of txs: 6.25 (range 1 to 8 txs) over 4 weeks (range 1 tx to 8 weeks; 2 with 1 yr FU)				2 high quality, 3 mod quality trials		**Grade of Evidence: B** (Man ther of the knee and/or full kinetic chain combined with multimodal or exercise therapy)	
Hillerman et al[74]	CT Allocation by presentation: PFPS, *<u>or</u>* PFPS + SI joint dysfnx	PFPS and quadriceps inhibition/ weakness	N=20 Age 18-40 = PFPS with and without SI	SI manipulation vs Knee axial elongation manipulation	<u>1 tx</u> Immediate FU No loss of patients	Significant ↑ in intra-group knee extensor strength by Cybex after SI manipulation		Int to Tx adequate	–
Drover et al[75]	CT Not randomized Focus: effect on knee extensors	PFPS (AKPS)	N=9 Mean Age 25.7	ART technique for Knee vs testing normal contra lateral leg	1 tx Immediate FU No loss of patients	No Significant change for all measures: 1.Knee extension strength Biodex. 2.mm inhibition: interpolated twitch torque technique		Int to Tx adequate	–
Crossley et al[53]	RCT Double blind	PFPS	N=71 Age ≤ 40	PT (patellar mobilization tape, exercise, stretch, soft tissue) vs Placebo (detuned ultrasound, tape, gel)	<u>6 txs</u> over 6 weeks 6 weeks. 3 mo FU PT group only	Significantly in favor of PT group VAS, AKPS, step ups. No serious adverse effects. Side effects: soreness in 2 in PT and in Placebo		Adequate power, Adequate blinding Int to tx reported	**++**

Suter et al[76]	**RCT** **Double blind**	**PFPS (AKPS)**	N=25 Mean Age 34	HVLA Sacroiliac manipulation only for PFPS vs Control – no adjustment Both measured for Muscle Inhibition (MI), EMG and mm strength in quadriceps	1 tx Immediate post tx follow up No loss of patients	Pre Tx baseline Significant decrease in MI by 7.5% using interpolated twitch torque technique (non significant ↑ in quad mm strength Cybex and EMG		Int to Tx adequate SI relieves PFPS knee pain	**++**
Rowlands and Brantingham[77]	RCT Single blind	PFPS	N=30 Ave Age >18 Some drop outs – not noted	Mob of patella vs Placebo (detuned ultrasound)	8 txs/ 4 weeks 1 month FU 2 month study	Significant in favor of mob: ↓ pain with Algometry and ↓ pain with McGill vs Placebo		McGill % intergroup change very large mob vs placebo >80% power; (McGill correlates well 0-100 scales). Algometry <power	**+**
Stakes et al[78]	RCT^ Single blind (see § below)	PFPS	N=60 Mean Age 30.5	Patellar mob vs Patellar mob and HVLA Sacroiliac or L/S adjustment	6 txs over 4 weeks 8 drop outs: 2 per group transport problems - No side effects. 2 per group lost to follow up. Subjects replaced.	No difference between groups. Power not calculated; inter-group statistics must be viewed with caution. Significant intra-group change for both groups: NRS, PFJE, SFMPQ, PSFS and Algometry		For both groups, magnitude of changes in NRS and PFJE scales % - appear statistically and clinically meaningful.	**+**
Taylor and Brantingham[79]	RCT (see § below) Blind assessor No unblinding	PFPS	N=12 Age Mean 30.17	Patellar mob vs Patellar mob + home exercise	8 txs over 4 weeks 1 week follow up. No side effects. All patients finished tx.	Descriptive statistics suggests both txs helpful. Non-parametric intra-group significant for NRS, SFMPQ, ALG and PSFS		Int to tx adequate	**+**
Level of evidence for Manipulative therapy for Patellofemoral Pain Syndrome (*aka:* Ant. Knee Pain Syndrome)		Average no. txs: 4.43 txs (2 trials 6 txs, 2 - 8 txs; Range 1 to 8 txs) over 4 to 8 weeks (Range 1 tx to 3 mo FU).				2 high quality, 2 moderate, 2 low quality trials		**Grade of Evidence: B** (Man ther of the knee and/or full kinetic chain combined with multimodal or exercise therapy)	

Ankle									
Pellow and Brantingham[80]	RCT Single blind	Ankle Sprain Subacute and chronic Grade I and II > 5 days	N=30 Mean Age 24.9	Manipulation ankle axial elongation (HVLA) vs Detuned ultrasound (placebo)	8 txs (or til sx free)/4 weeks 1 month FU 2 months	Significant for man ther for SFMPQ, functional improvement, at 8th tx, and for SFMPQ, functional, ROM 1 mo FU vs Placebo		Power adequate for intra-group No intention to treat	+
Green et al[55]	RCT^ Blind assessor	Ankle Sprain Acute (72 hours)	N=41 Mean Age 25.5	RICE and tape and A-P talus mob vs control (RICE and tape)	≤ 6 txs/ 2 weeks No adverse effects. No drop outs.	Significant for man ther for ↑ ROM, ↓ pain, ↑ Gait. Faster recovery, activity with mob		Adequate blinding Intention to tx adequate	+
Coetzer et al[81]	RCT^ § Retrospective2nd Blind assessor for motion palpation	Ankle Sprain Acute ≤24 hours	N=30	Both groups received (for ethical and methodological reasons) standard care= RICE. Man ther: HVLA ankle manipulation - axial elongation and subtalar joint eversion vs NSAID (Piroxicam)	6 txs /2 weeks with 1 mo FU NSAIDS 40mg 2 days-20mg 5 days With 1 mo FU	No significant difference between groups except 6th tx ↑ ROM in favor man ther; & blind assessor detected ↓ restricted motion in joints in man ther group at FU All groups had significant intragroup improvement: ALG (↓pain), Goniometer (↑ROM), NRS (↓pain), Athletic Limitation ↑ function) and SFMPQ (↓pain)		Power generally low Otherwise essentially equal effects	+
Eisenhart Et al[32]	RCT^ Single blind	Ankle Sprain Acute Grade I and II <24 hours	N=55 MeanAge 30.5 >18	Standard Care (RICE + NSAIDS) vs Standard Care + Osteopathic manipulative Therapy (OMT)	1 tx pre and post measures in ER. 1 wk FU Loss of patients n=15	Significant for man ther post 1st tx for ↓ swelling, ↓ VAS. 1 wk/ FU: Significant for man ther ↑ ROM dorsiflexion		Int to tx performed	+
Collins et al[82]	RCT Double blind	Ankle Sprain Subacute Grade II	N=16 Mean Age 28.5	Mobilization with movement (MWM) vs Placebo (sham) or Control (hold position)	1 tx pre and post All txs Drop outs discussed 2 left trial, 1 ↑ pain.	Man ther Significant for ROM ↑ dorsiflexion No change in PPT (Algometry) or TPT (Thermal pressure threshold)		2 left trial, 1 had increased pain. Int to tx not reported	+

Vicenzino et al[83]	RCT Random to 3 txs Double blind	Ankle Sprain Chronic recurrent < 20 mm dorsiflexion in injured ankle inclusion	N=16 Mean Age 19.8	1. MWM wt bearing post talar glide (PTG) and dorsiflexion ROM (DF) 2. Ditto but non-wt bearing 3. Control – position held	<u>1 tx</u> Immediate post tx FU No loss of patients	Significant for man ther ↑ PTGº and DFº weight bearing and non wb MWM Large effect sizes PTG, Mod effect ↑ dorsiflex vs control		Int to tx adequate	**++**
Lopez-Rodriguez et al[84]	RCT Single blind	Ankle sprain Grade II > 5 days	N=52 Mean age 22.5	Manipulation ankle axial elongation (HVLA) and Supine HVLA A-P talar thrust vs Placebo/control (holding position)	<u>1 tx</u> Immediate post tx or post placebo No loss of patients	Significantfor man ther ↑ in proprioception with Stabiliometry and Baropodometry vs placebo		Int to tx adequate	**+**
Kohne et al[85]	RCT^ (see § below) Baseline characteristics and statistics essentially equal (see Kohne, E dissertation)	Ankle Sprain Chronic recurrent Grade I and II	N=30 Mean Age 31.7	Manipulation ankle axial elongation (HVLA) Group 1, 6 txs vs Group 2 (control), 1 tx	<u>6 txs</u> /4 wks 1 wk FU vs 1 tx A "few" sensed ↑ "instability" in Group 1 (in – Kohne dissertation)	Significant for Group 1 (6 txs) for ↑ Proprioception and ↑ dorsiflexion ROM: ROM: strapped inclinometer ankle moved only by patient - ↓ bias			**+**
Level of evidence for Manipulative therapy for Ankle Inversion Sprain		Average txs: 3.75 txs (3 trials- 6 txs; 1 - 8 txs; 4 -1 tx; range 1 to 8 txs) over 2 to 8 weeks				1 high quality, 5 moderate, 2 low quality trials		**Grade of Evidence: B** (Man ther for ankle sprain with multimodal or exercise therapy)	
Foot									
Plantar fasciitis									
Dimou et al[87]	RCT^ Randomization (see § below) And blind assessor	Plantar Fasciitis Chronic > 7 weeks	N=20 Mean Age 42.4	Foot and ankle adjusting + stretching vs orthotics	<u>8 txs</u>/5 weeks 1 mo Follow up 2 months All patients Completed treatment	Significant ↓ pain between groups in NRS at 4 weeks in favor of man ther and stretching Significant (intragroup) for both txs (but not different) at 9 weeks for ↓ 1st step pain, ↓heel pain at rest and algometry		Int to treat adequate Low power No side effects	**+**
Level of evidence for Manipulative therapy for Plantar Fasciitis		Average txs: 8txs over 5 weeks				1 moderate quality trial		**Grade of Evidence: C** (Man ther for plantar fasciitis with stretch/and or multimodal/ exercise therapy)	

Metatarsalgia									
Petersen et al[89]	CT ¥ Systematic assignment (1st patient randomized)	Metatarsalgia (common or mechanical)	N=40 Mean Age 49.5	Man ther of foot and ankle (mob, HVLA: especially intermetatarsal glide, 1st MTPJ, etc) vs Placebo (detuned ultrasound)	8 txs/ 4 weeks 4 drop outs Not clear which groups; none from side effects	Significant in favor for man ther vs placebo for: SFMPQ, NRS, FFI and ALG. Note: placebo patients started with higher level of pain.			–
Govender et al[90]	RCT Single blind (see § below)	Morton's neuroma (aka Morton's metatarsalgia)	N=40 Mean Age 51	Adjustive therapy (mob and HVLA) for foot and ankle Vs Placebo (detuned ultrasound)	6 txs over 3 weeks All 20 finished trial. No drop outs. Side effects not reported.	Significantly in favor for man ther: NRS and Algometry Vs placebo		Power adequate Int to tx adequate	+
Level of evidence for Manipulative therapy for Metatarsalgia		Average txs: 7.5 txs over 3-4 wks. 1 trial 8txs – 1 – 6txs.				1 moderate quality trial 1 poor quality trial		**Grade of Evidence: C** (Man ther for metatarsalgia with/and without multimodal therapy)	
Hallux Limitus/Rigidus									
Shamus et al[92]	RCT^	Hallux Limitus	N=20 MeanAge 32.8	Man ther of hallux and or/hallux and sesamoids + different physical therapy protocols: Comparative tx: modalities, hallux mob, exercise) vs Experimental tx (same) + *sesamoid mob, hallux flex strengthening/ gait retraining*	12 txs/ 4 weeks No drop outs 2 patients discharged at 10 visits (with relief)	Significant in favor of Experimental tx for: ↑ ROM, ↑ strength, ↓ VAS, faster return of ROM and function		Single blind (blind patients) Int to Tx Adequate	+
Level of evidence for Manipulative therapy for Hallux Limitus/Rigidus		12 tx/4 weeks				1 moderate trial quality		**Grade of Evidence: C** (Man ther for hallux limitus/rigidus with multimodal therapy)	

Hallux Abducto Valgus (HAV or Bunion)									
Brantingham et al[95]	RCT Single blind	Hallux Abducto Valgus (HAV) (painful HAV)	N=60 Ave Age 50.1	Man ther of hallux, foot and ankle (with a progressive protocol of mobilization to HVLA manipulation of the hallux) vs Placebo (PT modality: non-therapeutic Action Potential Therapy)	6 txs /3 weeks. 1 week follow up 7 weeks total Drop outs not reported/unclear No reported side effects.	Significant in favor for man therapy for ↓ NRS, ↓pain, disability, ↑ function with HAL and FFI vs Placebo			+
Level of evidence for Manipulative therapy for Hallux Abducto Valgus/Bunion		6 txs/3 weeks				1 moderate trial (no other known trials, case series or case studies)		**Grade of Evidence: I** (Man ther for hallux abducto valgus)	

Definitions: *RCT*: a randomized controlled trial (treatment versus placebo), *RCT^* : a randomized clinical trial (treatment versus another treatment; usually comparative treatment demonstrated superior to placebo or, standard care). *CT*[¥]: a controlled or clinical trial with systematic assignment (*pseudo*-randomization) or non-randomization, but with inclusion, exclusion, controlled, independent and dependent variables versus placebo and/or comparative treatment. For the SIGN checklist rating (++, +, -) and a summary of grading strength of evidence (A, B, C, and I) see Tables 1 and 2.

Table 4. A summary of research on the hip: case series* [37-39]

Author	Diagnosis	Treatment/Management	Reported outcome
MacDonald et al[67]	Hip Osteoarthritis (HOA) N=7 Median age 62	Man ther of hip (grade IV and V) + exercise for (HOA) 5 treatments (over 2-5 weeks) 1. HVLA axial elongation 2. various hip manipulation and mobilization techniques from multiple sources/textbooks 3. Hip, knee and trunk exercises for hip OA	Harris Hip Scale (HHS for disability). 6 patients: median improvement ↑ 25 points (clinically meaningful {*clm*} change = ↑ 4 points). 1 patient (no HHS scale) but instead Global Rating of Change Scale: " a great deal better" 7 patients mean NPRS (↓ 5 points on 0-10 scale; *clm* 1.5 - 2 points) Goniometry: Global ↑ ROM 82º Conclusion: All ↓ pain, ↑ ROM

* Case series were assessed using the checklist for case series

Table 5. A summary of research on the knee: case series*

Author	Diagnosis	Treatment/Management	Reported outcome
Cliborne et al[72]	Knee Osteoarthritis (KOA) N= 22 with KOA (mean age 61) N=17 normal and asymptomatic (age 64) Does hip mobilization ↓ pain and ↑ ROM in KOA. What hip tests, etc + in both groups (Faber, hip ROM, Scour test, etc)	Man ther of hip (grade III and IV Maitland techniques) 1 treatment – immediate post test 1 group intragroup pre-post test	NPRS ↓ and all clinical tests less painful (except hip flexion) in mobilization group post test *p< 0.05* All clinical tests more + in KOA patients compared to normal asymptomatic, and less painful in symptomatic post test, except Faber)
Currier et al [73]	Knee Osteoarthritis (KOA) N=60 (51-79 yrs) Clinical Prediction Rule (CPR): study to determine which KOA variabres (patients) respond to hip mob and the validity of tests to predict outcome. 5 variables: 1. hip/groin pain or parathesia 2. Anterior thigh pain 3. Knee flexion < 122º 4. Hip internal rotation < 17º 5. pain with hip distraction	Man the of hip (Maitland grade IV) + exercise 4 treatments Immediate and 48 hour post test. 1 group intragroup pre-post test	Global Rating of change Scale ↑ 3.27points (clinically meaningful) NPRS, WOMAC, PSFS post test intragroup changes all statistically and clinically meaningful *p<0.05* *CPR in symptomatic KOA* *If + 2 CPRs 97% at 48 hour follow up (LR 5.1)* *If + 1 CPR 68% at 48 hours* *Conclusion: CPR may improve exam and treatment of KOA*

* For case series, the co-chairs of the CCGPP Scientific Commission developed a checklist modified from other instruments.

Table 6. A summary of research on the ankle and foot: case series*

Author	Diagnosis	Treatment/Management	Reported outcome
Dananberg et al[86]	Ankle Equinus (AE) N=22 (= abnormal loss of ankle dorsiflexion ROM ↓ less than 10º from neutral) 2nd diagnosis along with AE: a. plantar fasciitis b. acute chronic ankle sprain strain c. Achilles tendonitis d. neuroma e. metatarsalgia	Man ther + exercise (1 treatment manipulation and mobilization) 1 group immediate pre-post test 1. P-A HVLA manipulation to proximal fibular head 2. Traction (mob) ankle/mortice: axial elongation with HVLA A-P talar thrust 3. Then active dorsi/plantarflexion ROM movement of ankle by patient	Gravity goniometer strapped on and used only by patient (to ↓ bias): active ROM, patient pulling strap under foot, etc. Mean ↑ ankle dorsiflexion ROM 4.9º (left), 5.5º (right) *t*-tests at 99% confidence level *p<0.001* Reports soreness in some ≤ 2 days but none later States better than stretch alone
Dananberg HJ[50]	Ankle Equinus N=3 With: 1. Inversion sprain – chronic (and had big toe pain too) 2. Kohlers (osteochodrosis of the navicular with pain) 3. Hallux limitus (1st MTPJ stiffness and pain) All patients had ankle equinus + additional diagnosis	Man ther + various treatments per condition: RICE, taping, exercise (Inversion sprain), casting (Kohlers) orthotics (Hallux limitus) 1. Same as 2000 study plus: 2. manipulation of the 1st metatarsocuneiform joint for 1st MTPJ for ↓big toe pain.	3 week follow up for all. Descriptive outcomes. Ankle sprain (and big toe pain) 1 treatment resolved condition. ↑ ROM Kohler 's disease – A few treatments: quickly resolved navicular pain. Antalgia resolved. Hallux limitus. A few treatments ↓ Pain ↑ ROM of big toe.
Jennings and Davies[51]	Cuboid syndrome: unresolved lateral ankle/cuboid pain N=7 Mean age 21. 1 years old a. 2nd to inversion ankle sprain All college athletes and/or sports injuries	Man ther– HVLA "cuboid-whip" manipulation Different patients received additional treatments: tape, stretch, orthotics, modalities. 5 had 1 manipulation 2 had 2 manipulations	VAS pre and post (pre Average VAS 2.85 and post treatment VAS 0) Improvements post tx: also in ↓ cuboid tenderness, MTJ mobility, antalgic gait and in ability to do single hop
Wyatt L Et al[52]	Plantar fasciitis (recalcitrant lateral plantar pain, post fasciotomy – referred by podiatric surgeon for chiropractic after full post surgical healing and 4 -6 weeks of NSAIDS, shoe padding and rest) 15 patients Mean age 46.4 y/o None lost to FU	Man ther + multimodal a. manipulation and mobilization of the ankle and foot (including HVLA plantar to dorsal "snap or whip" manipulation. b. Exercise and change or ↓ activity c. 1tx/per week for 2-8 visits over 2-8 weeks.	Verbal Rating Scale (0-100) Most experienced quick relief 11 experienced significant or 90% relief on VRS 3 moderate relief (50-90%) 1 no change 9 had minor side effects to man ther which resolved

Solan et al[93]	Hallux Rigidus grades I-III (refers to x-ray findings) N=37 Mean age 52.3 years old 2 lost to follow up 1 year follow up 29 available	1 Man ther under anesthesia with steroid injection of the 1st MTPJ. <u>1 manipulation of hallux</u> (manipulative technique not fully described) 1 year follow up. No additional treatment: additional manipulation, exercise, stretch, medication, etc.	Relief was defined as: period of time free of symptoms = pain and stiffness on walking/using foot, and in activities of daily living/function and or making a decision to have surgery. Grade I = 6 months of relief Grade II = 3 months of relief Grade III = minimal to no relief. 12 grade I, 4 went to surgery 18 grade II, 12 went to surgery 5 grade 3, all 3 went to surgery Conclusion: manipulation acceptable for grade I, limited for grade II, not indicated grade III

* For case series, the co-chairs of the CCGPP Scientific Commission developed a checklist modified from other instruments.

Table 7. A summary of research on the hip/foot: case studies (descriptive)

Author	Diagnosis	Treatment/Management	Reported outcome
Whipple et al[69]	1. Acetabular anterosuperior labral tear 2. Instability (↑ ext. rot.) 3. Non-specific hip pain 1 patient 1 patient with symptoms for 1 month. 14 year old ballet dancer A. overstretch. B. weight-bearing flexed/extended twist of hip dancing C. painful click with abduction	Man ther 1 treatment 1. Cyriax technique (variation on technique for loose bodies): a. Axial elongation traction of the hip with b. 5 mobilizations from 30 to 75º abduction	Began VAS 7/10 with pain abducting when dancing. After treatment VAS 0/10 with abduction a. no pain on scour test b. ↑ external rotation persisted 1 week follow up no symptoms 6 month follow up – 1 incidence of "giving way" otherwise no symptoms 1 visit
Pollard et al[68]	1. Acetabular anterosuperior labral tear (arthroscopically confirmed) 2 patients 1. 45 y/o female. Prolonged housecleaning 3 weeks earlier (with 10 years of chronic mechanical LBP). 2. 15 y/o swimmer with 3 weeks of knee and groin pain	Man ther and mobilization (using multimodal and "MIMG" protocol –see paper) Patient 1 - 10 visits/2 months Patient 2 - 14 visits/2 ½ months a. hip long axis traction with HVLA variations b. other hip manipulations and mobilizations c. PNF, exercise, SMT, knee manipulative therapy, and activity modifications	Patient 1 ↓ hip pain 70%. Some pain with weight-bearing and rotation of hip ↓ CMLBP 80-90% Patient 2 initially ↓ hip pain 30%, at 3 and 6 months follow up 0% (no) hip pain. Painless click Hip ROM still partially ↓ Surgical consult – but surgeon recommends against at this time. 10-14 visits
Costa and Dyson et al[88]	Plantar fasciitis 1 patient. 15 y/o girl. Soccer injury. Knee and groin pain. Symptoms for 1 year even after treated by GP and podiatrist – minimal help.	Man ther + multimodal ther: a. manipulation and mobilization b. iontophoresis (acetic acid), orthotics, ice, tape, myofascial, exercise, stretch and activity changes and therapy, etc. 3x/week for 2 weeks the 2x/week for 2 weeks or 10 total treatments	Treatment began VAS 7/10 morning pain and 4/10 usual pain all day After 6 weeks of treatment resolution of symptoms 0/10 10 visits

Brantingham et al[94]	Hallux Rigidus (grade I) 1 patient 31 year old male professional golfer Big toe pain and stiffness for 7 months.	Man ther + multimodal ther: (all grades I-V) a. Hallux, ankle/foot, sesamoid mob and manip d. exercise therapy and stretching e. ultrasound Quick relief after a few txs 17 visits /10 months	NPRS 6/10 Lower extremity functional index (LEFI) 22% (0-100, 100 worst), hallux dorsiflexion ROM 45º Final visit NPRS 1-2/10 LEFI 2% Hallux dorsiflexion ROM 84º
Cashley[91]	Plantar digital neuritis (Morton's metatarsalgia) Aka: Morton's neuroma 2 patients Patient 1. 25 year old. Symptoms 3 months after soccer. Patient 2. 63 year old. 1 yr symptoms. Steroid injections /orthotics with minimal relief.	Man ther Patient 1: 4 txs plantarflexion HVLA manipulation at the MTPJs Patient 2: 3 txs over 6 weeks.	Descriptive Patient 1 pain free by 4 weeks. Follow up at 14 months still pain and symptom free Patient 2 pain free after 3 treatments. Follow up at 8 months still pain and symptom free

Discussion

This literature review revealed new, recent and previously non-cited (secondary to limitations previously discussed) peer-reviewed papers and publications regarding manipulative treatment; for the most part with, but also without adjunctive therapy (frequently exercise and/or rehabilitation and soft-tissue therapy, secondarily, in conjunction with modalities, NSAIDS, etc) for lower extremity conditions. Since the Hoskins et al 2006 review, and enabled with broader inclusion parameters, there is a clear increase of limited and fair evidence for use of manipulative therapy in the treatment of a number of common lower extremity disorders. Notably, within this new evidence, there exist several studies representing higher level evidence with case studies and series of increasing quality continuing to proliferate. Also worth noting is that the highly rated trials, included in this analysis have recently been included into systematic reviews for treatments of hip and knee osteoarthritis, patellofemoral pain syndrome, and inversion sprain. Interestingly as well, this proliferation of competing, systematic reviews, using a variety of methodologies, perplexingly, reach opposite conclusions as to whether to support or *not support* the same treatment. One surprising example of just such a finding is *exercise* for acute inversion sprain.[33,36,96,97,98] Nevertheless, overall, when reviewing the increasing quantity and quality of included trials, manipulative therapy for lower extremity disorders appears to be of value and like spinal manipulative therapy is fundamentally safe. The trials and studies utilized numerous outcome measures, most with minimally general, and some with a condition-specific validity and reliability, such as: primary patient report of improvement (using Likert and other scales), Algometry, Visual Analogue and Numerical Pain Rating Scales, the Short-form McGill Pain Questionnaire, Cybex isokinetic muscle testing, Goniometry, the Anterior Knee Pain Scale, Harris Hip Scale, Western Ontario and McMasters Arthritis Index, Hallux Metatarsophalangeal Interphalangeal Index, Foot Function Index, Interpolated Twitch and EMG, and Functional tests like “First Step Heel Pain”, “Step-Ups”, “Get Up and Go”, Gait Analysis, Stabiliometry, Baropodometry as well as orthopedic tests.

The literature now suggests vigorous and sustained interest in the application of peripheral or extremity manipulative therapy for lower extremity conditions (and updated epidemiological data is needed in this area); conveying the impression that the examination and usefulness of manipulative therapy procedures for lower extremity disorders has barely begun. There are trials and/or studies for hip osteoarthritis, knee osteoarthritis, patellofemoral pain syndrome, ankle sprain (acute and chronic), plantar fasciitis, metatarsalgia, Morton’s neuroma, hallux limitus, hallux valgus; with case series and studies assessing hip manipulative therapy (with exercise) for hip osteoarthritis, knee manipulative therapy *for* hip osteoarthritis, the effect of hip manipulative therapy *for* knee osteoarthritis, ankle and/or foot manipulative therapy for treatment of ankle equinus, metatarsalgia, Achilles tendonitis, plantar fasciitis, Morton’s metatarsalgia, and hallux manipulation and injection for treatment of hallux rigidus, foot and ankle manipulative therapy for “cuboid syndrome” secondary to lateral ankle sprains, and other and various additional case studies demonstrating the momentum, growing interest and publication in this area. *In effect, the present studies of manipulative*

therapy for lower extremity disorders appear to parallel the results and overall beneficial outcomes per spinal research.[99,100,101] While it will be useful to thoroughly investigate the most effective methods of manipulation/mobilization for each and every joint in the human body, at this point, based upon the combined level of evidence of the benefit of mobilization/manipulation for the axial and appendicular system as well as safety, one could tentatively posit that, in the presence of mechanical joint dysfunction and other applicable signs and symptoms, joint mobilization/manipulation appears to be universally indicated for lower limb joints as a therapeutic trial, in combination with other reasonable evidence-influenced conservative approaches, and for all common neuromusculoskeletal joint conditions, particularly where joint hypomobility is suspected as contributory. Common indications for the use of a manipulative therapy (characterized by various definitions such as joint dysfunction, subluxation or, as a result of a clinical prediction rule) are: 1) diagnosis of a painful neuromusculoskeletal joint disorder 2) pain in or from palpation of bony joint surfaces 3) pain in or from palpation of joint soft tissues 4) decreased or altered range or quality of motion 5) pain on stressing and/or over-stressing/provoking (in any or all planes) a joint. [2,73,72,83,102,103]

Clearly, chiropractors are highly trained practitioners in the utilization of HVLA thrusting techniques, but the profession has used low velocity, high or low amplitude mobilization techniques throughout the last century; and a myriad of mobilization techniques are well represented and employed within the profession and these studies.[1,2,8,78 79,90] As noted, most manipulative therapy applied to extremity disorders is delivered as multi-modal therapy, blending exercise, soft tissue treatment, modalities, or multiple extremity joint and/or combined spinal and extremity joint manipulative therapy (treatment of the kinetic chain), usually condition and patient-specific.[1,16,78,79,54,72,73] In fact it would appear that manipulative therapy with stretch is superior to either alone in increasing range of motion, a possible solution to a previous conundrum of reductionistic interventional study.[16,21,70,71] Further research should address issues of safety, clinical predictors of efficacy and effectiveness, clarification of scope, and similar issues.

Limitations

The main limitation of this review is that, as with all reviews, some studies may have potentially been missed or were omitted for a priori reasons. For example, a study would have been missed if it did not contain the included search terms or key words or was simply not contained within the applicable/normative databases. . Studies without a *peripheral diagnosis* (for example, measuring ROM), RCTs utilizing *immediate* rehabilitative post surgical manipulative therapy of an extremity, conference proceedings, red flag conditions or conditions that required referral were excluded.[1,104,105,106,107] Unfortunately, this means that interesting and informative studies such as an RCT of osteopathic manipulative treatment immediately following knee and/or hip arthroplasty, manipulative management of foot pain due to an os peroneum and accessory navicular, spinal manipulative therapy for a hamstring injury (without clear *peripheral* injury and diagnosis) and chiropractic management of injuries sustained during Brazilian capoeira (art that fuses dance, sport and martial arts) were unfortunately not included.[107,52, 108,109,110] Future reviewers may want to consider including immediate (or rehabilitative) post surgical manipulative therapy management.

Conclusion

There is a growing number of peer reviewed, published studies of manipulative therapy for lower extremity disorders.
There is a level of **C** or limited evidence for manipulative therapy combined with multimodal or exercise therapy for hip osteoarthritis, a level of **B** or fair evidence for manipulative therapy of the knee and/or full kinetic chain, combined with multimodal or exercise therapy for knee osteoarthritis and patellofemoral pain syndrome. There is a level of **B** or fair evidence for manipulative therapy of the ankle and/or foot combined with multimodal or exercise therapy for ankle inversion sprain. There is a level of **C** or limited evidence for manipulative therapy of the ankle and/or foot combined with multimodal or exercise therapy for plantar fasciitis, metatarsalgia and hallux limitus/rigidus. There is also a level of **I** or insufficient evidence for manipulative therapy of the ankle and/or foot combined with multimodal or exercise therapy for Hallux Abductor Valgus or Bunion. These are preliminary findings representing some of the first published peer reviewed studies. Additional, larger, methodologically improved and well funded randomized controlled and clinical trials, as well as observational, clinical and basic science research, case series and studies are both needed and merited. Interdisciplinary collaboration should certainly be encouraged and supported as well. Finally, The basic overarching model of similarity of indications for and beneficial effect/responsiveness of patients to manipulative therapies for joint conditions through out the human body merits further attention.

References

1. Hoskins W, McHardy A, Pollard H, Windsham R, Onley R. Chiropractic treatment of lower extremity conditions: a literature review. *J Manipulative Physiol Ther.* Oct 2006;29(8):658-671.

2. Peterson D, Bergmann T. *Chiropractic technique: principles and procedures*. 2nd ed. St. Louis, Missouri: Mosby; 2002p97-169,184.

3. Christensen M, Kollasch M, Ward R, Kelly R, Day A, zumBrunnen J. *Job analysis of chiropractic 2005*. Greeley, Colorado: National Board of Chiropractic Examiners; 2005p67-100.

4. Nelson C, Lawrence D, Triano J, et al. Chiropractic as spine care: a model for the profession. *Chiropr Osteopat.* Jul 2005 13:9.

5. Finn AM, MacAirt J. A survey of the work practices of physiotherapists in the community. *Ir J Med Sci.* Feb 1994;163(2):61-64.

6. Cherkin DC, Sherman KJ. Acupuncture and knee osteoarthritis. *Ann Intern Med.* May 17 2005;142(10):872; author reply 872-873.

7. Brantingham JW, Snyder WR. Old Dad Chiro and extravertebral manipulation. *Chiropr Hist.* Dec 1992;12(2):8-9.

8. Wardwell W. *Chiropractic History and the evolution of a new profession*. St. Louis, MO: Mosby; 1992 p90.

9. Keating J, Brantingham J, Donahue J, Brown R, Toomey W. A brief history of manipulative foot care in America. *Chiropr Techn.* 1992;4(3):90-103.

10. Barnes P, Powell-Griner E, McFann K, Nahin R. Complementary and alternative medicine use among adults: United States, 2002. *Adv Data.* 2004;27(343):1-19.

11. Pollard H, Hoskins W, McHardy A, et al. Australian chiropractic sports medicine: half way there or living on a prayer? *Chiropr Osteopat.* 2007;15:14.

12. Metz RD, Nelson CF, LaBrot T, Pelletier KR. Chiropractic care: is it substitution care or add-on care in corporate medical plans? *J Occup Environ Med.* Aug 2004;46(8):847-855.

13. Brantingham J. *Foundational studies in manipulative therapy for lower extremity neuromusculoskeletal disorders [PhD dissertation].* European Institute of Health and Medical Sciences, University of Surrey, Guildford, England; 2005.

14. Mootz R, Cherkin D, Odegard C, Eisenberg D, Barassi J, Deyo R. Characteristics of chiropractic practitioners, patients, and encounters in Massachusetts and Arizona. *J Manipulative Physiol Ther.* Nov-Dec 2005;28 (9):645-653.

15. Cherkin D, Deyo R, Sherman K, et al. Characteristics of visits to licensed acupuncturists, chiropractors, massage therapists, and naturopathic physicians. *J Am Board Fam Pract.* Nov-Dec 2002;15(6):463-472.

16. Hoeksma HL, Dekker J, Ronday HK, et al. Comparison of manual therapy and exercise therapy in osteoarthritis of the hip: a randomized clinical trial. *Arthritis Rheum.* Oct 15 2004;51(5):722-729.

17. van Baar ME, Dekker J, Oostendorp RA, et al. The effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: a randomized clinical trial. *J Rheumatol.* Dec 1998;25(12):2432-2439.

18. Palmer B, Palmer D. *The science of chiropractic*. Davenport: Palmer School of Chiropractic; 1906p14,358.

19. Palmer D. *The chiropractors adjustor*. Portland: Portland Publishing; 1910p787.
20. Vaux P. Hip osteoarthritis: a chiropractic approach *Euro J Chiropr* 1998;46(1):17-22.
21. Brantingham J, Williams A, Parkin-Smith G, Weston P, Wood T. A controlled, prospective pilot study into the possible effects of chiropractic manipulation in the treatment of osteoarthritis of the hip. *Euro J Chiropr.*2003(51):149-166.
22. Brantingham J, Snyder W. Did osteopathy 'borrow' the chiropractic short lever adjustment (the core of all modern manipulation techniques) without giving Palmer credit? . *Chiro Hist* 1997;17(1):41-50.
23. Cyriax J. *Textbook of orthopaedic medicine*. 7th ed. London: Bailliere Tindall; 1978p595-621.
24. Grieve G. *Common vertebral joint problems*. Edinburgh, Scotland: Churchill-Livingston; 1981p451-67.
25. Moseley J, O'Malley K, Petersen N, et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med.* 2002;347(2):81-88.
26. Lauretti W. *Comparative safety of chiropractic. In: Redwood D, Cleveland C; Fundamentals of chiropractic*. Louis, MI: Mosby; 2003p581-580.
27. McGettigan P, Henry D. Cardiovascular risk and inhibition of cyclooxygenase: a systematic review of the observational studies of selective and nonselective inhibitors of cyclooxygenase 2. *JAMA.* Oct 4 2006;296(13):1633-1644.
28. Bennell KL, Hinman RS, Metcalf BR, et al. Efficacy of physiotherapy management of knee joint osteoarthritis: a randomised, double blind, placebo controlled trial. *Ann Rheum Dis.* Jun 2005;64(6):906-912.
29. Moss P, Sluka K, Wright A. The initial effects of knee joint mobilization on osteoarthritic hyperalgesia. *Man Ther.* May 2007;12(2):109-118.
30. Menz H. Manipulative therapy of the foot and ankle: science or mesmerism? *The Foot* 1998;8:68-74.
31. Guler-Uysal F, Kozanoglu E. Comparison of the early response to two methods of rehabilitation in adhesive capsulitis. *Swiss Med Wkly.* Jun 12 2004;134(23-24):353-358.
32. Eisenhart AW, Gaeta TJ, Yens DP. Osteopathic manipulative treatment in the emergency department for patients with acute ankle injuries. *J Am Osteopath Assoc.* Sep 2003;103(9):417-421.
33. van der Wees P, Lenssen AF, Hendriks EJ, Stomp DJ, Dekker J, de Bie RA. Effectiveness of exercise therapy and manual mobilisation in ankle sprain and functional instability: a systematic review. *Aust J Physiother.* 2006;52(1):27-37.
34. Cyriax J. *Illustrated manual of orthopedic medicine*. 2nd ed. London: Butterworth-Heinemann Medical; 1996p91-110.
35. Bergmann T, Peterson, DH, Lawrence, DL. *Chiropractic Prinicples and Procedures*. New York: Churchill Livingstone; 1993p523-722.
36. Zhang W, Moskowitz R, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis and Cartilage.* 2008;16:137-162.
37. Scottish Intercollegiate Guidelines Network. A Guideline Developers' Handbook. Edinburgh: SIGN , 2001.

38. Harbour R, Miller J. A new system for grading recommendations in evidence based guidelines. *Br Med J.* Aug 11 2001;323(7308):334-336.
39. Liddle J, Williamson M, Irwig L. Method for evaluating research and guideline evidence (MERGE). Sydney: New South Wales Department of Health.1996
40. United States Department of Health and Human Services. Agency for Health Care Policy and Research. Acute pain management: operative or medical procedures and trauma. Rockville, MD: AHCPR, 1993:107. (Clinical practice guideline No 1, AHCPR publication No 920023.).
41. Haldeman S, Chapman-Smith D, Petersen D. Guidelines for Chiropractic Quality Assurance and Practice Parameters. Paper presented at: Proceedings of a consensus conference commissioned by the Congress of Chiropractic State Associations, 1993p103-177; Mercy Conference Center. Gaithersburg, MD.
42. Greenman P. *Principles of manual medicine*. 2nd ed. Baltimore: Lippincott Williams and Wilkins; 1996p3-52.
43. Maitland G. *Peripheral manipulation*. 3rd ed. Reed Education and Professional Publishing Ltd; 1999p9-52.
44. Domholdt E. *Physical therapy research: principles and applications*. 2nd ed. ed. Philiadelphia: W. B Saunders Company; 2000 p98,106
45. Portney L, Watkins P. *Foundations of clinical research: applications to practice*. 2nd ed. ed. New Jersey: Prentice-Hall; 2000p142
46. Haneline M. *Evidence-Based Chiropractic Practice*. Sudbury, Massachusetts: Jones and Bartlett Publishers, Inc; 2007p 173-175.
47. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. *Phys Ther.* Aug 2003;83(8):713-721.
48. Jadad A, Moore R, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: Is blinding necessary? *Controlled Clin Trials.* 1996;17(1):1-12.
49. Neuhauser D, Diaz M. Shuffle the deck, flip that coin: randomization comes to medicine. *Qual Saf Health Care.* Aug 2004;13(4):315-316.
50. Dananberg HJ. Manipulation of the ankle as a method of treatment for ankle and foot pain. *J Am Podiatr Med Assoc.* Jul-Aug 2004;94(4):395-399.
51. Jennings J, Davies G. Treatment of cuboid syndrome secondary to lateral ankle sprains: a case series. *J Orthop Sports Phys Ther.* July 2005;35(7):409-415.
52. Wyatt LH. Conservative chiropractic management of recalcitrant foot pain after fasciotomy: a retrospective case review. *J Manipulative Physiol Ther.* Jun 2006;29(5):398-402.
53. Crossley K, Bennell K, Green S, Cowan S, McConnell J. Physical Therapy for Patellofemoral Pain. A Randomized, Double-Blinded, Placebo- Controlled Trial. *Am J Sports Med.* 2002;30(6):857-865.
54. Deyle G, Henderson N, Matekel R, Ryder M, Barber M, Allison S. Effectiveness of manual physical therapy and exercise in osteoarthritis of the knee. *Ann Intern Med.* 2000;132(1):173-180.
55. Green T, Refshauge K, Crosbie J, Adams R. A randomized controlled trial of a passive accessory joint mobilization on acute ankle inversion sprains. *Phys Ther.* Apr 2001;81(4):984-994.

56. Altman D, Schulz K, Moher D, et al. The revised CONSORT statement for reporting randomized trials: explanation and elaboration. *Ann Intern Med.* 2001;134(8):663-694.
57. Kirby A, Gebski V, Keech AC. Determining the sample size in a clinical trial. *Med J Aust.* Sep 2 2002;177(5):256-257.
58. Peto R, Pike M, Armitage P, et al. Design and analysis of randomized clinical trials requiring prolonged observation of each patient. *Br J Cancer.* 1976;34:585-612.
59. Armitage P. Attitudes in clinical trials. *Stat Med.* Dec 15 1998;17(23):2675-2683.
60. Gail MH. Eligibility exclusions, losses to follow-up, removal of randomized patients, and uncounted events in cancer clinical trials. *Cancer Treat Rep.* Oct 1985;69(10):1107-1113.
61. Sandler RS, Halabi S, Baron JA, et al. A randomized trial of aspirin to prevent colorectal adenomas in patients with previous colorectal cancer. *N Engl J Med.* Mar 6 2003;348(10):883-890.
62. Hollis S, Campbell F. What is meant by intention to treat analysis? Survey of published randomised controlled trials. *Bmj.* Sep 11 1999;319(7211):670-674.
63. Gravel J, Opatrny L, Shapiro S. The intention-to-treat approach in randomized controlled trials: are authors saying what they do and doing what they say? . *Clin Trials.* 2007;4(4):350-356.
64. Porta N, Bonet C, Cobo E. Discordance between reported intention-to-treat and per protocol analyses. *J Clin Epidemiol.* Jul 2007;60(7):663-669.
65. Baron G, Boutron I, Giraudeau B, Ravaud P. Violation of the intent-to-treat principle and rate of missing data in superiority trials assessing structural outcomes in rheumatic diseases. *Arthritis Rheum.* Jun 2005;52(6):1858-1865.
66. *Handbook for the Preparation of Explicit Evidence-Based Clinical Practice Guidelines*; New Zealand Guidelines Group. Greer N MG, Logan A, Halaas G; A Practical Approach to Evidence Grading, Joint Commission Journal on Quality Improvement, 2001;26: 700-712, 2000.
67. MacDonald C, Whitman J, Cleland J, Smith M, Hoeksma H. Clinical outcomes following manual physical therapy and exercise for hip osteoarthritis: A case series *J Orthop Sports Phys Ther.* Aug 2006;36(8):588-599.
68. Pollard H, Hoskins W, Schmerl M. The use of hip manipulation in the management of acetabular labrum injury. *Chiropr J Aust.* 2007;37:49-56.
69. Whipple T, Plafcan D, Sebastianelli W. Manipulative treatment of hip pain in a ballet student: a case study. *J Dance Med Sci.* 2004;8(2):53-55.
70. Deyle GD, Allison SC, Matekel RL, et al. Physical therapy treatment effectiveness for osteoarthritis of the knee: a randomized comparison of supervised clinical exercise and manual therapy procedures versus a home exercise program. *Phys Ther.* Dec 2005;85(12):1301-1317.
71. Tucker M, Brantingham J, Myburg C. The relative effectiveness of a non-steroidal anti-inflammatory medication (meloxicam) versus manipulation in the treatment of osteoarthritis of the knee *Euro J Chiropr* 2003;50(3):163-184.
72. Cliborne AV, Wainner RS, Rhon DI, et al. Clinical hip tests and a functional squat test in patients with knee osteoarthritis: reliability, prevalence of positive test

findings, and short-term response to hip mobilization. *J Orthop Sports Phys Ther.* Nov 2004;34(11):676-685.

73. Currier LL, Froehlich PJ, Carow SD, et al. Development of a clinical prediction rule to identify patients with knee pain and clinical evidence of knee osteoarthritis who demonstrate a favorable short-term response to hip mobilization. *Phys Ther.* Sep 2007;87(9):1106-1119.

74. Hillermann B, Gomes A, Korporaal C, Jackson D. A pilot study comparing the effects of spinal manipulative therapy with those of extra-spinal manipulative therapy on quadriceps muscle strength. *J Manipulative Physiol Ther.* Feb 2006;29(2145-9).

75. Drover JM, Forand DR, Herzog W. Influence of active release technique on quadriceps inhibition and strength: a pilot study. *J Manipulative Physiol Ther.* Jul-Aug 2004;27(6):408-413.

76. Suter E, McMorland G, Herzog W, Bray R. Decrease in quadriceps inhibition after sacroiliac joint manipulation in patients with anterior knee pain. . *J Manipulative Physiol Ther.* 1999;22(3):149-153.

77. Rowlands B, Brantingham J. The efficacy of patella mobilisation in patients suffering from patellofemoral pain syndrome. *JNMS.* 1999;7(4):142-149.

78. Stakes N, Myburgh C, Brantingham J, Moyer R, Jensen M, Globe G. A Prospective Randomized Clinical Trial to Determine Efficacy of Combined Spinal Manipulation and Patella Mobilization Compared to Patella Mobilization Alone in the Conservative Management of Patellofemoral Pain Syndrome. *J Amer Chiropr Assoc* 2006;43(7):11-18.

79. Taylor K, Brantingham J. An investigation into the effect of exercise combined with patella mobilisation/manipulation in the treatment of patellofemoral pain syndrome. *Euro J Chiropr* 2003;51(1):5-17.

80. Pellow JE, Brantingham JW. The efficacy of adjusting the ankle in the treatment of subacute and chronic grade I and grade II ankle inversion sprains. *J Manipulative Physiol Ther.* Jan 2001;24(1):17-24.

81. Coetzer D, Brantingham J, Nook B. The relative effectiveness of piroxicam compared to manipulation in the treatment of acute grades 1 and 2 inversion ankle sprains. *JNMS.* 2001;9(1):1-12.

82. Collins N, Teys P, Vicenzino B. The initial effects of a Mulligan's mobilization with movement technique on dorsiflexion and pain in subacute ankle sprains. *Man Ther.* May 2004;9(2):77-82.

83. Vicenzino B, Branjerdporn M, Teys P, Jordan K. Initial changes in posterior talar glide and dorsiflexion of the ankle after mobilization with movement in individuals with recurrent ankle sprain. *J Orthop Sports Phys Ther.* Jul 2006;36(7):464-471.

84. Lopez-Rodriguez S, Fernandez de-Las-Penas C, Alburquerque-Sendin F, Rodriguez-Blanco C, Palomeque-del-Cerro L. Immediate effects of manipulation of the talocrural joint on stabilometry and baropodometry in patients with ankle sprain. *J Manipulative Physiol Ther.* Mar-Apr 2007;30(3):186-192.

85. Köhne E. *To determine the immediate efficacy of manipulation on proprioception in chronic ankle instability syndrome in terms of objective clinical findings. M.Tech: Chiropractic dissertation*. Durban, South Africa, Durban University of Technology; 2005.

86. Dananberg HJ, Shearstone J, Guillano M. Manipulation method for the treatment of ankle equinus. *J Am Podiatr Med Assoc.* Sep 2000;90(8):385-389.
87. Dimou E, Brantingham J, Wood T. A randomized, controlled trial (with blinded observer) of chiropractic manipulation and Achilles stretching vs orthotics for the treatment of plantar fasciitis. *J Amer Chiropr Assoc.* 2004;41(9):32-42.
88. Costa I, Dyson A. The integration of acetic acid iontophoresis, orthotic therapy and physical rehabilitation for chronic plantar fasciitis: a case study. *JCCA.* 2007;51(3):166-174.
89. Petersen S, Brantingham J, Kretzmann H. The efficacy of chiropractic adjustment in the treatment of primary metatarsalgia. *Euro J Chiropr* 2003;49(3):267-279.
90. Govender N, Kretzmann H, Price J, Brantingham J, Globe G. A single-blinded randomized placebo-controlled clinical trial of manipulation and mobilization in the treatment of Morton's neuroma. *J Amer Chiropr Assoc.* Apr 2007;44(3):9-18.
91. Cashley D. Manipulative therapy in the treatment of plantar digital neuritis (Morton's metatarsalgia). *Br J Podiatr.* 2000;3(3):67-69.
92. Shamus J, Shamus E, Gugel RN, Brucker BS, Skaruppa C. The effect of sesamoid mobilization, flexor hallucis strengthening, and gait training on reducing pain and restoring function in individuals with hallux limitus: a clinical trial. *J Orthop Sports Phys Ther.* Jul 2004;34(7):368-376.
93. Solan MC, Calder JD, Bendall SP. Manipulation and injection for hallux rigidus. Is it worthwhile? *J Bone Joint Surg Br.* Jul 2001;83(5):706-708.
94. Brantingham J, Chang M, Gendreau D, Price J. The effect of chiropractic adjusting, exercises and modalities on a 32-year old professional male golfer with hallux rigidus: a case report. *Clin Chiropr.* June 2007;10(2):91-96.
95. Brantingham J, Guiry S, Kretzmann H, Globe G, Kite V. A pilot study of the efficacy of a conservative chiropractic protocol using graded mobilization, manipulation and ice in the treatment of symptomatic hallux abductovalgus bunions. *Clin Chiropr.* 2005;8(3):117-133.
96. Dixit S, DiFiori J, Burton M, Mines B. Management of patellofemoral pain syndrome. *Am Fam Physician.* Jan 15 2007;75(2):194-202.
97. Ivins D. Acute ankle sprain: an update. *Am Fam Physician.* Nov 15 2006;74(10):1714-1720.
98. Kerkhoffs G, Handoll H, de Bie R, Rowe B, Struijs P. Surgical versus conservative treatment for acute injuries of the lateral ligament complex of the ankle in adults. *Cochrane Database Syst Rev.* 2007(2):CD000380.
99. Bronfort G, Haas M, Evans R, Kawchuck G, Dagenais S. Evidence-informed management of chronic low back pain with spinal manipulation and mobilization. *Spine.* 2008;8(1):213-225.
100. Carroll LJ, Cassidy JD, Peloso PM, et al. Methods for the best evidence synthesis on neck pain and its associated disorders: the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine.* Feb 15 2008;33(4 Suppl):S33-38.
101. Hurwitz EL, Carragee EJ, van der Velde G, et al. Treatment of neck pain: noninvasive interventions: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine.* Feb 15 2008;33(4 Suppl):S123-152.

102. Gibbons P, Tehan P. *Manipulation of the spine, thorax and pelvis: an osteopathic perspective.* . London: Churchill Livingstone 2000p5-8.
103. Degenhardt B, Snider K, Snider E, Johnson J. Interobserver reliability of osteopathic palpatory diagnostic tests of the lumbar spine: improvements from consensus training. *J Am Osteopath Assoc.* Oct 2005;105(10):465-473.
104. Fryer GA, Mudge JM, McLaughlin PA. The effect of talocrural joint manipulation on range of motion at the ankle. *J Manipulative Physiol Ther.* Jul-Aug 2002;25(6):384-390.
105. Nield S, Davis K, Latimer J, Maher C, Adams R. The effect of manipulation on the range of movement at the ankle joint. *Scan J Rehabil Med.* 1993;25:161-166.
106. Pollard H, G. W. The effect of upper cervical or sacroiliac manipualtion on hip flexion range of motion. *J Manipulative Physiol Ther.* 1998;21(9):611-616.
107. Licciardone JC, Stoll ST, Cardarelli KM, Gamber RG, Swift JN, Jr., Winn WB. A randomized controlled trial of osteopathic manipulative treatment following knee or hip arthroplasty. *J Am Osteopath Assoc.* May 2004;104(5):193-202.
108. Requejo S, Kulig K, Thordarson D. Management of foot pain associated with accessory bones of the foot: two clinical case reports. *J Orthop Sports Phys Ther.* 2000;30(10):580-594
109. Hoskins WT, Pollard HP. Successful management of hamstring injuries in Australian Rules footballers: two case reports. *Chiropr Osteopat.* Apr 12 2005;13(1):4.
110. Wessely M, Scheel L. Chiropractic management of injuries sustained during brazilian capoeira (conference proceedings). *J Chiropr Edu.* 2006;20(1):111.