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COST-EFFECTIVENESS OF MANUAL THERAPY FOR THE MANAGEMENT OF MUSCULOSKELETAL CONDITIONS: A SYSTEMATIC REVIEW AND NARRATIVE SYNTHESIS OF EVIDENCE FROM RANDOMIZED CONTROLLED TRIALS

Alexander Tsertsvadze, MD, MSc,a Christine Clar, PhD,a Rachel Court, MA,b Aileen Clarke, MD,c Hema Mistry, PhD,d and Paul Sutcliffe, DPhil,e

ABSTRACT

Objectives: The purpose of this study was to systematically review trial-based economic evaluations of manual therapy relative to other alternative interventions used for the management of musculoskeletal conditions.

Methods: A comprehensive literature search was undertaken in major medical, health-related, science and health economic electronic databases.

Results: Twenty-five publications were included (11 trial-based economic evaluations). The studies compared cost-effectiveness and/or cost-utility of manual therapy interventions to other treatment alternatives in reducing pain (spinal, shoulder, ankle). Manual therapy techniques (eg, osteopathic spinal manipulation, physiotherapy manipulation and mobilization techniques, and chiropractic manipulation with or without other treatments) were more cost-effective than usual general practitioner (GP) care alone or with exercise, spinal stabilization, GP advice, advice to remain active, or brief pain management for improving low back and shoulder pain/disability. Chiropractic manipulation was found to be less costly and more effective than alternative treatment compared with either physiotherapy or GP care in improving neck pain.

Conclusions: Preliminary evidence from this review shows some economic advantage of manual therapy relative to other interventions used for the management of musculoskeletal conditions, indicating that some manual therapy techniques may be more cost-effective than usual GP care, spinal stabilization, GP advice, advice to remain active, or brief pain management for improving low back and shoulder pain/disability. However, at present, there is a paucity of evidence on the cost-effectiveness and/or cost-utility evaluations for manual therapy interventions. Further improvements in the methodological conduct and reporting quality of economic evaluations of manual therapy are warranted in order to facilitate adequate evidence-based decisions among policy makers, health care practitioners, and patients. (J Manipulative Physiol Ther 2014;37:343-362)

Key Indexing Terms: Cost-Effectiveness; Cost-Utility; Manual Therapy; Systematic Review; Back Pain; Chiropractic

Man:ual therapy is a skilled nonsurgical conservative management using the practitioner’s hands and/or fingers on the patient’s body for the purpose of assessing, diagnosing, and treating a variety of symptoms and conditions.1,2 Manual therapy is used within the traditional medical (eg, physiotherapy, orthopedics, and...
sports medicine) and complementary and alternative medicine context (eg, chiropractic and osteopathy) and consists of different techniques (eg, manipulation, mobilization, static stretching, and muscle energy techniques). The definition and purpose of manual therapy vary across health care professionals.

The use of manipulation and mobilization has been recommended in clinical practice guidelines in the United States, Great Britain, Canada, and the Netherlands.\(^3\)–\(^9\) Although past research evidence on the clinical effectiveness \(^10\)–\(^19\) and safety \(^20\)–\(^27\) of manual therapy relative to other interventions is abundant, the evidence on cost-effectiveness is insufficient and inconclusive.\(^28\)–\(^30\) Moreover, to our best knowledge, a systematic review of full economic evaluations of recent evidence (ie, cost-effectiveness [CEA] and/or cost-utility analysis [CUA]) alongside randomized controlled trials (RCTs) of manual therapy has not been conducted.

In light of limited health care resources, policy makers, health care providers, and researchers need to make informed decisions in prioritizing and allocating resources to the provision of health care interventions that are both effective and cost saving. Ideally, the decision-making process should be based on high-quality evidence summarizing incremental costs and effects of a health care intervention of interest compared with alternative interventions.

The aim of this review was to systematically identify, appraise, and evaluate the evidence on trial-based economic evaluations (cost-effectiveness and/or cost-utility) of manual therapy relative to other alternative interventions used for the management of musculoskeletal conditions.

**Methods**

This review is part of a large technical report of comparative benefits and harms of manual therapy interventions for the management of musculoskeletal and nonmusculoskeletal conditions, commissioned by the Royal College of Chiropractors in the United Kingdom (http://www2.warwick.ac.uk/fac/med/research/hscience/pet/reportforcollegeofchiropractors/).

A comprehensive literature search was undertaken as part of a wider search for this report. The following medical, health-related, science and health economic electronic databases were searched (through August 2011): MEDLINE (Ovid), Embase, Mantis, Index to Chiropractic Literature, CINAHL, Cochrane Airways Group trial register, Cochrane Complementary Medicine Field register, and Cochrane Rehabilitation Field register (via CENTRAL), Science Citation Index, AMED, CDSR, National Health Service (NHS) DARE, NHS HTA, NHS EED, CENTRAL, ASSIA, and Social Science Citation Index. The search strategy used in MEDLINE is provided in Appendix 1. Search terms were restricted to subject heading and free-text terms related to manual therapy. Broader terms such as “physiotherapy” were not included because initial tests suggested that the volume of the literature identified using such a broad search strategy would not be manageable. To keep the search as open as possible, no condition terms were included. The search was limited to the study types included in the wider report by the use of recognized search filters, including the NHS Centre for Reviews and Dissemination NHS EED filter (see: http://www.crd.york.ac.uk/). This performance of this filter has been tested.\(^37\) No date limits were applied. The search results were updated on February 15, 2013. Additional studies were sought through references of relevant primary studies and systematic reviews.

This review included English-language full-text publications of RCTs that evaluated the cost-effectiveness and/or cost-utility of manual therapy (eg, manipulation, mobilization, static stretching, chiropractic care, muscle energy techniques alone or in combination) compared with alternative interventions (eg, no treatment, placebo, and usual care) used for the management of musculoskeletal conditions. We defined musculoskeletal conditions as disorders of muscles, nerves, tendons, ligaments, joints, cartilage, and spinal disks that develop over time. They can be categorized as spinal (eg, mid, low back or neck pain, sciatica, and headaches), upper extremity (eg, shoulder disorders, carpal tunnel syndrome, and lateral epicondylitis), and lower extremity (eg, ankle sprain) disorders.

We excluded studies where manual therapy was used to treat acute injuries such as fractures and dislocations (eg, to realign bones), except when used for rehabilitation purposes. Studies reporting only costs, only outcomes, reviews, protocols, and conference abstracts were excluded. Cost-consequence studies were excluded because they present an array of different outcomes and cost measures. Studies for which there was insufficient information to calculate the incremental cost-effectiveness ratios (ICERs) for CEA or CUA were also excluded.

Two independent reviewers (A.T. and P.S.) screened all identified bibliographic records for title/abstract and then for full text. Any disagreements were resolved through consensus or by recourse to a third-party reviewer (A.C.). The first author independently extracted relevant data from included studies which was checked by another reviewer (P.S.). The extracted data included study characteristics (eg, author name, country, year of publication, sample size, and follow-up duration), types of participants (eg, condition, age, and sex), types of interventions/comparators, type of economic analysis (cost-effectiveness, cost-utility), perspective (societal, health care system, individual), study currency, discounting, and information pertinent to risk of bias (ROB)/study quality assessment items. The outcomes included pain/disability scores, quality of life (QOL) measures, quality-adjusted life-years (QALYs), costs, and ICERs. We converted mean costs to UK £2012 prices using country-specific gross domestic product deflators\(^38\) and Purchasing Power Parities from Organisation for Economic Co-operation and Development (€1 = US $1.45 in 2012 prices).\(^39\) We calculated ICERs for each study, if not
reported directly. We chose a single willingness to pay (WTP) threshold of £20,000 to £30,000, which is currently used for the National Institute for Health and Care Excellence (NICE).

The methodological and reporting quality of economic analyses of the included studies were assessed using the Drummond 10-item checklist. This tool helps to assess the following domains: (a) adequacy of research question, (b) description of treatments, (c) identification of costs and consequences, (d) measurement of costs and consequences, (e) valuation and adjustment of costs and consequences for different timing, (f) incremental analysis of costs and consequences of alternative treatments, (g) uncertainty in the estimates of costs and consequences, and (g) presentation and discussion of study results and issues of concern.

The ROB in relation to clinical outcomes (ie, pain and health-related QOL measures) was assessed using the 11-item checklist of internal validity criteria recommended by the Cochrane Back Review Group. This tool is designed to assess the following domains of bias per each outcome: (a) selection bias (ie, methods of randomization and allocation concealment, similarity of groups in important prognostic factors at baseline), (b) performance bias (ie, blinding of patients and care providers, similarity of interventions across study groups), detection bias (ie, blinding of outcome assessors), and attrition bias (ie, noncompliance, dropouts, and intention-to-treat analysis). Based on the number of satisfied criteria (response: yes), the studies were assigned a low (at least 6 criteria satisfied) or a high (5 or fewer criteria satisfied) ROB. This threshold was selected given the empirical evidence showing that trials satisfying at least 6 criteria reported smaller effect sizes than trials satisfying fewer criteria (5 or less). In support of this construct, the previous research has demonstrated that studies of low methodological quality (ie, higher ROB) tend to exaggerate the treatment effects.

The results were organized by condition and, within each condition, by type of manual therapy. The results were summarized in text and tables.

**Results**

We initially identified 25,539 (16,976 after de-duplication) bibliographic records, of which 1014 were included in the technical report through the 2-stage screening process (abstract/title and full text). The updated search contributed additional 229 potentially relevant records. Thus, a total of 1243 records were screened for the cost-effectiveness review, of which 129 passed at title/abstract screening level and were judged to be potentially relevant for full-text review. One hundred four of the 129 publications were excluded at full text (these included studies that reported information on costs [n = 31] or outcomes [n = 9], and CUsAs where not enough information was provided to calculate the ICER [n = 2]). Figure 1 provides full details of the search results and reasons for exclusion. The remaining 25 publications, representing 11 unique RCTs included in the review, were the following: Bosmans et al, Williams et al, the UK Back Pain Exercise and Manipulation (BEAM) trial team 2004, Niemisto et al, Rivero-Arias et al, Bergman et al, Whitehurst et al, Korthals-de Bos et al, Lewis et al, Lin et al, and Critchley et al.

The study, participant, treatment, methodology, and outcome characteristics for the 11 included trials are presented in Table 1. The studies were conducted in the United Kingdom, the Netherlands, Finland, and Australia. The sample size ranged from 94 to 1334 participants. Duration of follow-up ranged from 6 to 24 months. The mean age of participants ranged from 37 to 51 years. The participants presented with spinal pain (low/upper back, neck), low back pain, neck pain, shoulder pain, and ankle fractures. Most studies included participants with nonspecific pain (ie, patients with spinal/shoulder pathology, rheumatoid arthritis, malignancies, pregnancy, osteoarthritis, psychiatric disease, or herniated disk were excluded). In the reviewed studies, interventions whose main components included manual therapy techniques (eg, manipulation and mobilization) were compared with usual general practitioner (GP) care, GP advice, physiotherapist advice, pain management program (back pain education, strengthening, stretching, aerobic exercise), exercise, physiotherapy (postural relaxation, walking exercises), or advice and exercise (A&E). Most interventions lasted from 6 to 12 weeks. The cost-effectiveness analyses were based on pain intensity and disability measures. The utility for QALY was based on the EuroQoL EQ-5D (European Quality of Life–5 Dimensions) or the Assessment of Quality of Life (AQoL). The perspective of economic evaluations was societal or health care system. All studies from a societal perspective included direct medical, direct nonmedical, and indirect costs. Given 12 months of follow-up in most studies, no discounting was undertaken (see Table 1).

**Methodological and Reporting Quality of Economic Evaluations**

The quality assessment showing the percentage of items with “yes” on the Drummond checklist is presented in Table 2. In all studies, the research question was clearly formulated, with good descriptions of the interventions and comparators. Most studies reported all important costs (ie, direct medical, direct nonmedical, and indirect) and consequences (ie, outcome measures). Because costs were not individually itemized for more than half of the studies, it was not clear what data were...
used to calculate the total costs. All studies reported valuation methods of costs and consequences, which were judged as adequate. The ICERs were reported in all studies, except for 1 study where information was provided to calculate this ratio.\textsuperscript{67,68} The studies provided detailed discussion sections by highlighting main study findings, interpretation of the findings, study strengths and limitations, consistency of findings with other studies, and future directions.

**Risk of Bias Assessment**

Risk of bias assessments are presented in Table 3. Briefly, 7 of the 11 included trials were rated as having low ROB\textsuperscript{45,50,53,57,61,67,69} and 4 trials as having high ROB.\textsuperscript{48,55,63,65} Patients and care providers in the studies were not blinded to the intervention type, and because the outcomes were self-reported (eg, pain, QOL), blinding of assessors was considered not applicable. Most of the studies reported adequate methods of randomization and treatment allocation concealment. Results of all studies were based on intention-to-treat analysis.

**Cost-Effectiveness and/or Cost-Utility of Manual Therapy**

Results are presented by condition in the text below as well as in Table 4.

**Spinal Pain (Low Back, Upper Back, and/or Neck).** In a trial by Williams et al\textsuperscript{48,49} the addition of osteopathic manipulation to usual GP care was more costly compared with...
Table 1. Included RCTs and Their Characteristics

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Study Participants</th>
<th>Study Perspective Type of Costs Methods</th>
<th>Interventions (Components)</th>
<th>Outcome Measures</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sample size</td>
<td>Perspective: National Health Service</td>
<td>Intervention 1: OSM</td>
<td>Mean QALY (based on quality of life score</td>
<td></td>
</tr>
<tr>
<td>Spinal (upper/lower back, neck, or both) pain</td>
<td>201 patients</td>
<td>Direct medical costs: GP and outpatient consultations, investigations, prescribing, hospital stay</td>
<td>(osteopathic manipulation + advice on keeping active, exercise regularly, and avoiding excessive rest) + usual GP care [3-4 sessions]</td>
<td>EuroQoL EQ-5D</td>
<td>6 months</td>
</tr>
<tr>
<td>Williams 2004 UK</td>
<td>(randomised), 136 patients (analysed)</td>
<td>Direct non-medical costs: NA</td>
<td>Intervention 2: Usual GP care [3-4 sessions]</td>
<td>ICER</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age (mean): 44 years</td>
<td>Indirect costs: NA</td>
<td>Intervention 3: Pain management (back pain education, strengthening, stretching, aerobic exercise, cognitive behavioural approach) [8 sessions]</td>
<td>[12 sessions]</td>
<td>18 months</td>
</tr>
<tr>
<td></td>
<td>Male (%): 50</td>
<td>Discounting: None</td>
<td>Duration: NR</td>
<td>Mean QALY (based on quality of life score</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inclusion: patients aged ≥18 years referred by GP with non-specific LBP ≥12 weeks</td>
<td>Mean QALY (based on quality of life score</td>
<td>ICER</td>
<td>[3-4 sessions]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exclusion: previous spinal surgery, PT for LBP within 6 months prior to enrolment, chronic conditions such as rheumatoid arthritis or disabilities rendering unsuitable for the treatment</td>
<td>EuroQoL EQ-5D</td>
<td>[8 sessions]</td>
<td>[8 sessions]</td>
<td></td>
</tr>
<tr>
<td>Low Back Pain</td>
<td>Sample size: 212 patients</td>
<td>Perspective: National Health Service</td>
<td>Intervention 1: Individual</td>
<td>Mean QALY (based on quality of life score</td>
<td></td>
</tr>
<tr>
<td>Critchley 2007 UK</td>
<td>(randomised), 148 patients (analysed)</td>
<td>Direct medical costs: Hospital stays and visits, staff time, procedures, investigations</td>
<td>PT (joint manipulation, mobilisation, massage, back care advice, individual exercises including trunk muscle retraining, stretches, and general spinal mobility)</td>
<td>EuroQoL EQ-5D</td>
<td>18 months</td>
</tr>
<tr>
<td></td>
<td>Age (mean): 44 years</td>
<td>Direct non-medical costs: NA</td>
<td>Intervention 2: spinal stabilisation PT (transverses abdominis and lumbar multifidus muscle training, exercise for spinal stability) [8 sessions]</td>
<td>ICER</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Male (%): 50</td>
<td>Indirect costs: NA</td>
<td>Intervention 3: Pain management (back pain education, strengthening, stretching, aerobic exercise, cognitive behavioural approach) [8 sessions]</td>
<td>[12 sessions]</td>
<td>18 months</td>
</tr>
<tr>
<td></td>
<td>Inclusion: patients aged ≥18 years referred by GP with non-specific LBP ≥12 weeks</td>
<td>Discounting: 3.5%</td>
<td>Duration: NR</td>
<td>Mean QALY (based on quality of life score</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exclusion: previous spinal surgery, PT for LBP within 6 months prior to enrolment, chronic conditions such as rheumatoid arthritis or disabilities rendering unsuitable for the treatment</td>
<td>Mean QALY (based on quality of life score</td>
<td>[8 sessions]</td>
<td>EuroQoL EQ-5D</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exclusion: previous spinal surgery, PT for LBP within 6 months prior to enrolment, chronic conditions such as rheumatoid arthritis or disabilities rendering unsuitable for the treatment</td>
<td>Mean QALY (based on quality of life score</td>
<td>ICER</td>
<td>[8 sessions]</td>
<td></td>
</tr>
<tr>
<td>Niemisto 2005 Finland</td>
<td>Sample size: 204 patients (randomised), 138 patients (analysed)</td>
<td>Perspective: Societal</td>
<td>Intervention 1: Manipulative combination treatment (manipulation with muscle energy technique to correct any biomechanical dysfunction in the lumbar or pelvic segments, stabilizing exercise to correct the lumbopelvic rhythm, GP advice) [4 sessions]</td>
<td>ICER (based on pain and ODI scores)</td>
<td>24 months</td>
</tr>
<tr>
<td></td>
<td>Age (mean): 37 years</td>
<td>Direct medical costs: Physician visits, physiotherapy visits, outpatient clinics, hospital stays, x-rays</td>
<td>Intervention 2: GP advice (booklet, advice on exercise, muscle stretch, and stability) [1 session]</td>
<td>Mean QALY (based on quality of life score</td>
<td>24 months</td>
</tr>
<tr>
<td></td>
<td>Male (%): 46</td>
<td>Direct non-medical costs: Drug and travel costs</td>
<td>Duration: 4 weeks</td>
<td>EuroQoL EQ-5D</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inclusion: patients 24-46 years of age with non-specific LBP ≥3 months and disability measured with ODI of 16%</td>
<td>Indirect costs: Productivity loss costs</td>
<td>Duration: 4 weeks</td>
<td>ICER</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exclusion: malignancies, ankylosing spondylitis, severe osteoporosis, osteoarthritis, paralysis, progressive neurologic disorder, haemophilia, spinal infection, spinal operation, vertebral fracture within 6 months of trial, pregnancy, severe sciatica, and psychiatric disease</td>
<td>Discounting: None</td>
<td>Duration: 4 weeks</td>
<td>[4 sessions]</td>
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</tbody>
</table>

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Table 1. (continued)

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Sample size</th>
<th>Age (mean)</th>
<th>Male (%)</th>
<th>Inclusion</th>
<th>Exclusion</th>
<th>Interventions (Components)</th>
<th>Follow-up</th>
<th>Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rivera-Arias 2006 UK</td>
<td>286 patients (randomised and analysed)</td>
<td>41 years</td>
<td>47.5</td>
<td>≥ 18 years with LBP</td>
<td>Spinal surgery, or treatment for physical problems</td>
<td>Intervention 1: PT (articulatory mobilisation, manipulation, or soft tissue techniques, spinal mobilisation, back exercise, ergonomic advice, back education)</td>
<td>12 months</td>
<td>Mean QALY (based on EuroQol EQ-5D)</td>
</tr>
<tr>
<td>UK BEAM 2004 UK</td>
<td>1334 patients (randomised), 1287 patients (analysed)</td>
<td>43.1 years</td>
<td>44</td>
<td>≥ 1 months and RMDQ ≥ 4</td>
<td>Spinal surgery, or treatment for physical problems</td>
<td>Intervention 1: GP care</td>
<td>12 months</td>
<td>Mean QALY (based on EuroQol EQ-5D)</td>
</tr>
<tr>
<td>Whitehurst 2007 UK</td>
<td>402 patients (randomised and analysed)</td>
<td>41 years</td>
<td>47</td>
<td>≥ 18-65 years of age with non-specific LBP</td>
<td>Spinal surgery, or treatment for physical problems</td>
<td>Intervention 1: Manual PT</td>
<td>12 months</td>
<td>Mean QALY (based on EuroQol EQ-5D; RMDQ score)</td>
</tr>
<tr>
<td>Neck Pain Bosmans 2011 The Netherlands</td>
<td>146 patients (randomised and analysed)</td>
<td>45 years</td>
<td>40</td>
<td></td>
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Table 1. (continued)

<table>
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<tr>
<th>Study ID</th>
<th>Study Participants</th>
<th>Study Perspective Type of Costs Methods</th>
<th>Interventions (Components)</th>
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<th>Follow-up</th>
</tr>
</thead>
</table>
| Korthals-de Bos 2003 63,64 The Netherlands | **Inclusion:** patients 18-70 years of age with non-specific neck pain (4-12 weeks)  
**Exclusion:** malignancy, neurologic disease, herniated disc, or systemic rheumatic disease  
**Perspective:** Societal  
**Direct medical costs:** GP, SMT, PT, outpatient appointments, hospitalisation, exercise, home care  
**Direct non-medical costs:** Alternative therapy, home care, friend’s or partner’s help, travel  
**Indirect costs:** Absenteeism from paid/unpaid work  
**Discounting:** None (trial duration: 6 months)  
**Intervention 1:** SMT (combination of techniques described by Cyeriax, Kaltenborn, Maitland, and Mennel using hands-on muscular and articular mobilisation techniques, coordination or stabilisation techniques, and joint mobilisation with low-velocity passive movements) [6 sessions]  
**Intervention 2:** PT (active, postural, or relaxation exercises, stretching, massage, manual traction) [12 sessions]  
**Intervention 3:** GP care (standard care, advice on self-care, education, ergonomic issues, paracetamol or NSAIDs, if necessary) [1 session and optional biweekly follow-up visits]  
**Duration:** 6 weeks | | | Mean QALY ICER (based on EuroQoL EQ-5D; pain; NDI) | 12 months |
| Lewis 2007 65,66 UK | **Sample size:** 183 patients (randomised), 178 patients (analysed)  
**Age (mean):** 45 years  
**Male (%):** 40  
**Inclusion:** patients 18-70 years of age with non-specific neck pain (≥ 2 weeks)  
**Exclusion:** previous neck surgery, malignancy, neurologic disease, fracture, herniated disc, or systemic rheumatic disease  
**Perspective:** National Health Service and Societal  
**Direct medical costs:** Study intervention sessions, GP consultations, outpatient appointment (e.g., rheumatology, physiotherapist, neurologist, emergency, radiographer, acupuncturist)  
**Direct non-medical costs:** patient expenses (e.g., prescription drugs, over-the-counter medicines, devices)  
**Indirect costs:** Absenteeism from paid work  
**Discounting:** None (trial duration: 6 months)  
**Intervention 1:** A & E [8 sessions]  
**Intervention 2:** A & E + SMT (passive/active assisted hands-on movements, joint and soft tissue mobilisations or manipulations graded as appropriate to the patient’s signs and symptoms) [8 sessions]  
**Intervention 3:** A & E + PSWD [8 sessions]  
**Duration:** 6 weeks | | | Mean QALY ICER (based on EuroQoL EQ-5D; NPQ) | 6 months |

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### Table 1. (continued)

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Study Participants</th>
<th>Study Perspective Type</th>
<th>Costs Methods</th>
<th>Interventions (Components)</th>
<th>Outcome Measures</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Shoulder Pain</strong></td>
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</tr>
<tr>
<td>Bergman 2010</td>
<td>Sample size: 150</td>
<td>Societal</td>
<td>Direct medical costs:</td>
<td>SMT (high velocity low amplitude manipulation and passive low velocity mobilisation within the range of joint motion) [6 sessions] + usual GP care [advice on daily living, if needed analgesics, NSAIDs, corticosteroid injections, or PT including massage and exercise]</td>
<td>ICER (based on perceived recovery; shoulder pain; shoulder disability; general health)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>patients (randomised), 140 patients (analysed; excluding 2 outliers)</td>
<td></td>
<td>treatment by GP, physiotherapist, manual, occupational, exercise or complementary health therapists, visits to consultant in orthopaedic surgery, acupuncture, neurology, rheumatology, rehabilitation medicine, and hospitalisation</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Age (mean): 48</td>
<td></td>
<td>Direct non-medical costs:</td>
<td>out-of-pocket expenses, costs for paid/unpaid help</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>years Male (%): 49</td>
<td></td>
<td>Indirect costs:</td>
<td>loss of production due to sick leave from paid/unpaid work</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inclusion: patients ≥ 18 years with non-specific shoulder pain without shoulder treatment in the past 3 months</td>
<td></td>
<td>Discounting:</td>
<td>None</td>
<td></td>
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<tr>
<td></td>
<td>Exclusion: fractures, ruptures or dislocations in the shoulder region, previous orthopaedic surgery, contraindications for manipulative therapy, cervical nerve root compression, rheumatic disorder, dementia, psychiatric disorder, or abdominal pathology</td>
<td></td>
<td>Duration:</td>
<td>(trial duration: 6 months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ankle Fracture</strong></td>
<td>Sample size: 94</td>
<td>Health care system and patient</td>
<td>Direct medical costs:</td>
<td>outpatient physiotherapy, medical specialists, GP, emergency department, hospitalisation, medication, investigations, private health providers,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lin 2008</td>
<td>patients (randomised), 92 patients (analysed)</td>
<td></td>
<td>Direct non-medical costs:</td>
<td>public transport, private vehicle</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age (mean): 45.5</td>
<td></td>
<td>Anterior-posterior glides of the talus</td>
<td>[8 sessions]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>years Male (%): 54</td>
<td></td>
<td>PT including massage and gait retraining, walking aids, advice, ice, elevation and progression if required</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inclusion: patients ≥ 18 years with ankle fractures treated with cast immobilisation with cast removed the week before the trial entry, pain VAS ≥ 2, approved to weight-bear as tolerated or partial weight-bear</td>
<td></td>
<td>Intervention 1:</td>
<td>MT (large amplitude oscillatory motion) [6 sessions]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exclusion: patients with significant pathologies</td>
<td></td>
<td>Intervention 2:</td>
<td>PT [5 sessions]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Duration:</td>
<td>4 weeks</td>
<td></td>
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</tr>
</tbody>
</table>

A&E, advice and exercise; BGA, behavioral graded activity; BPM, brief pain management; EQ-SD, European Quality of Life-5 Dimensions; GP, general practitioner; ICER, incremental cost-effectiveness ratio; LBP, lower back pain; MRI, magnetic resonance imaging; MT, manual therapy; NA, not applicable; NDI, Neck Disability Index; NHS, National Health Service; NPQ, Northwick Park Neck Pain Questionnaire; NR, not reported; NS, statistically nonsignificant; NSAIDs, nonsteroidal anti-inflammatory drugs; ODI, Oswestry Disability Index; OSM, osteopathic manual therapy; PSWD, pulsed shortwave diathermy; PT, physiotherapy/physical therapy; QALY, quality-adjusted life year; RMDQ, Roland-Morris Disability Questionnaire; SMT, spinal manipulation therapy.

GP care alone (£402 vs £286). The associated ICER was £4674 per QALY gained. This estimate was lower than the threshold of £30,000 used by the NICE, suggesting the addition of osteopathic manipulation to usual GP care as a potentially cost-effective option for patients with spinal pain. **Low Back Pain.** In the study by Critchley et al., pain management dominated both individual physiotherapy and spinal stabilization physiotherapy. Individual physiotherapy was more effective and marginally more costly than spinal stabilization physiotherapy, with a mean ICER of £1279 per QALY gained.
The trial by Niemisto et al\textsuperscript{53,54} evaluated the cost-effectiveness of combination of manual therapy, stabilization exercise, and physician consultation compared with physician consultation alone in patients with low back pain. This study demonstrated significantly reduced pain intensity for the combination treatment compared with physician consultation alone at 24-month follow-up (visual analog scale [VAS] score: 30.7 vs 33.1, \textit{P} = .01). The associated ICER was £165 per score improvement on VAS and was £384 per score improvement on disability scale.

The trial by Rivero-Arias et al\textsuperscript{55,56} compared physiotherapy with physiotherapist advice in participants with low back pain. At 12 months of follow-up, physiotherapy was more expensive (£2320 vs £247) and more effective (QALYs gained: 0.74 vs 0.69) than the physiotherapist advice group, but neither the incremental mean costs nor the incremental mean QALYs between the 2 treatment groups was statistically significant. The cost per QALY gained was £1454. If the decision maker is willing to pay £5000, the most cost-effective treatment option for patients with low back pain was the addition of manipulation to GP care.

Whitehurst et al\textsuperscript{45,47} compared manual physiotherapy with a brief pain management program in patients with acute low back pain. At 12 months of follow-up, the mean cost per patient for the manual physiotherapy was greater compared with brief pain management, with a mean difference of £66. Although the gains in disability (Roland-Morris Disability Questionnaire [RMDQ] mean score, 0.33) and utility (mean QALYs, 0.022) were in favor of manual physiotherapy vs brief pain management, these differences were not statistically significant. The ICER for manual physiotherapy relative to brief pain management was £3006 per QALY gained. If the NHS were willing to pay £10 000 per QALY gained, there was 83% chance that manual physiotherapy relative to brief pain management was the most cost-effective treatment option for patients with low back pain.

Table 2. Methodological Quality of Economic Evaluations in the Included Studies (the Drummond Checklist for Critical Appraisal of Economical Evaluation)\textsuperscript{80}

<table>
<thead>
<tr>
<th>Item no.</th>
<th>Bergman et al\textsuperscript{7–40}</th>
<th>Bosmans et al\textsuperscript{11–40}</th>
<th>Critchley et al\textsuperscript{49}</th>
<th>Korthals-de Bos et al\textsuperscript{0.64}</th>
<th>Lewis et al\textsuperscript{0.66}</th>
<th>Lin et al\textsuperscript{57,68}</th>
<th>Niemisto et al\textsuperscript{3,54}</th>
<th>Rivero-Arias et al\textsuperscript{55,56}</th>
<th>UK BEAM\textsuperscript{30–52}</th>
<th>Whitehurst et al\textsuperscript{41,62}</th>
<th>Williams et al\textsuperscript{48,49}</th>
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<td>Item 1</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Can’t tell (costs)</td>
<td>Yes</td>
<td>No (costs)</td>
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<td>Can’t tell (costs)</td>
<td>Can’t tell (costs)</td>
<td>Can’t tell (costs)</td>
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<td>Can’t tell (costs)</td>
<td>Can’t tell (costs)</td>
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<td>Can’t tell (costs)</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Item 9</td>
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<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Item 10</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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</tbody>
</table>

\textit{% of items with “yes” on Drummond checklist}:

\begin{tabular}{|c|c|c|c|c|c|c|c|c|c|c|c|}
\hline
& 90 & 100 & 80 & 80 & 80 & 80 & 90 & 100 & 100 & 100 & 100 & 100 \\
\hline
\end{tabular}
effective than manual therapy in reducing pain intensity (ICER: £388 per improvement in pain score) and disability (ICER: £152 per improvement in disability score) but not for perceived recovery (ICER: £17,444 per improvement in recovery score).

One trial by Korthals-de Bos et al.63,64 evaluated manual therapy, physiotherapy, and GP care in patients with neck pain. After 1 year of follow-up, manual therapy was significantly less costly than physiotherapy (−£1149) and GP care (−£1260). Moreover, manual therapy was significantly more effective in reducing neck pain than physiotherapy (mean difference, 1.20), but not disability (mean difference, 0.90). The mean differences in pain intensity (0.10) and disability (−1.40) between manual therapy and GP care were not statistically significant. The manual therapy demonstrated dominance (both less costly and more effective) over both physiotherapy and GP care for perceived recovery and utility. Also, manual therapy was dominant over physiotherapy for pain intensity. Physiotherapy and GP care did not differ in either costs or in improving neck pain or disability.

Lewis et al.65,66 conducted an economic evaluation in which A&E plus manual therapy or pulsed shortwave diathermy was compared with A&E alone in patients with neck pain. At 6 months, the differences in costs, disability, and QALYs gained between the treatment groups were not statistically significant. In terms of societal perspective, for disability, the A&E plus manual therapy had a higher probability of being cost-effective (up to 55%) than A&E.

---

**Table 3. Risk of Bias Assessment of the Included RCTs (Adapted From van Tulder et al.41)**

<table>
<thead>
<tr>
<th>ROB Item</th>
<th>Bergman et al.7–60</th>
<th>Bosmans et al.45–47</th>
<th>Critchley et al.49</th>
<th>Korthals-de Bos et al.63,64</th>
<th>Lewis et al.65,66</th>
<th>Lin et al.67,68</th>
<th>Niemisto et al.53,54</th>
<th>Rivero-Arias et al.55,56</th>
<th>UK BEAM 50–52</th>
<th>Whitehurst et al.01,62</th>
<th>Williams et al.48,49</th>
</tr>
</thead>
<tbody>
<tr>
<td>Was the method of randomization adequate?</td>
<td>Don’t know</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Don’t know</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Don’t know</td>
</tr>
<tr>
<td>Was the treatment allocation concealed?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Don’t know</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Don’t know</td>
</tr>
<tr>
<td>Were the groups similar at baseline regarding the most important prognostic indicators?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Was the patient blinded to the intervention?</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Was the care provider blinded to the intervention?</td>
<td>Don’t know</td>
<td>Don’t know</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Don’t know</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Was the outcome assessor blinded to the intervention?</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Were cointerventions avoided or similar?</td>
<td>Don’t know</td>
<td>Don’t know</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Don’t know</td>
<td>Yes</td>
<td>No</td>
<td>Don’t know</td>
<td>Don’t know</td>
<td>Don’t know</td>
</tr>
<tr>
<td>Was the compliance acceptable in all groups?</td>
<td>Yes</td>
<td>No</td>
<td>Don’t know</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Don’t know</td>
<td>Don’t know</td>
<td>Don’t know</td>
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<tr>
<td>Was the dropout rate described and acceptable?</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Was the timing of the outcome assessment in all groups similar?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Did the analysis include an intention-to-treat analysis?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Yes, if item is satisfied; no, if item is not satisfied; Don’t know, unclear if item was satisfied or not; Low ROB, if 6 or more items are satisfied (rated as “yes”). High ROB, if 5 or fewer items are satisfied (rated as “yes”).

NA, not applicable; ROB, risk of bias.
Table 4. Cost-Effectiveness/Cost-Utility of Manual Therapy Interventions According to Condition – RCTs

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Analysis</th>
<th>Health Outcomes</th>
<th>Mean Costs</th>
<th>Mean (SD) Health Effects</th>
<th>Difference in Costs</th>
<th>Incremental Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Spinal (upper/lower back, neck, or both) pain</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>UK</td>
<td>Statistical analysis: Non-parametric bootstrap (1000 simulations)</td>
<td></td>
<td>Costs: £402</td>
<td></td>
<td>Health effects</td>
<td>EQ-5D: 0.717 (0.248)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>QALY: 0.056 (0.101)</td>
<td></td>
<td>Usual GP care</td>
<td>Costs: £286</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Health effects</td>
<td></td>
<td>EQ-5D: 0.656 (0.289)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>QALY: 0.031 (0.105)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Low Back Pain</strong></td>
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<tr>
<td>UK</td>
<td>Statistical analysis: ANOVA, non-parametric bootstrap (number of simulations: NR)</td>
<td></td>
<td>Costs: £574</td>
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<td>Health effects</td>
<td>EQ-5D: 0.67</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>QALY: 0.990</td>
<td></td>
<td>Spinal stabilisation PT</td>
<td>Costs: £459</td>
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<td>Health effects</td>
<td></td>
<td>EQ-5D: 0.63</td>
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<td></td>
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<td></td>
<td>QALY: 0.900</td>
<td></td>
<td>Pain management</td>
<td>Costs: £200</td>
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<td>Health effects</td>
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<td>EQ-5D: 0.68</td>
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<td></td>
<td></td>
<td>QALY: 1.000</td>
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<tr>
<td>Niemisto 2005</td>
<td>Analysis: CEA</td>
<td>Pain (visual analogue score), Oswestry Disability Index (ODI), 15-D (HRQoL)</td>
<td>MT + exercise + GP advice</td>
<td>Incremental Costs:</td>
<td>-£1075</td>
<td>£165</td>
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<td>Finland</td>
<td>Statistical analysis: Repeated measures ANOVA, Intention to Treat analysis, bootstrap technique (5000 simulations)</td>
<td>Costs: £4568</td>
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<td>Cost per unit of outcome improved in:</td>
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<td>Rivero-Arias 2006</td>
<td>Analysis: CUA</td>
<td>EuroQoL EQ-5D</td>
<td>PT</td>
<td>Incremental Costs:</td>
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<td>£1454</td>
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<td>UK</td>
<td>Statistical analysis: Mean differences and 95% CI using independent sample t test (for costs) and ANCOVA (for QALYs), multiple imputation for missing values using linear regression technique</td>
<td></td>
<td>Costs: £320</td>
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<td>Health effects</td>
<td>EQ-5D: 0.73 (0.25)</td>
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<td>QALY: 0.740 (0.18)</td>
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<td>Physiotherapist advice</td>
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<td>EQ-5D: 0.72 (0.26)</td>
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<td>QALY: 0.690 (0.23)</td>
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<td>UK BEAM 2004</td>
<td>Analysis: CUA</td>
<td>EuroQoL EQ-5D</td>
<td>GP (Best) care + manipulation</td>
<td>GP (Best) care + manipulation - GP (Best) care</td>
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<td>Costs: £702</td>
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<td>Health effects</td>
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<td>GP (Best) care + manipulation + exercise</td>
<td>GP (Best) care + manipulation + exercise - GP (Best) care</td>
<td>Incremental costs:</td>
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<td>Costs: £612</td>
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<td>Health effects</td>
<td>QALY: 0.651</td>
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| | | | GP (Best) care + exercise | GP (Best) care + exercise - GP (Best) care | Incremental costs: | £162 | | (continued on next page)
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<th>Mean Costs</th>
<th>Difference in Costs</th>
<th>Incremental Ratio</th>
<th>Mean (SD) Health Effects</th>
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<td>Dominant over GP (Best) care + exercise</td>
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<td>GP (Best) care + exercise - GP (Best) care Incremental costs:</td>
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<td>Manual PT</td>
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<td>Health effects</td>
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<td></td>
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<td>SMT (MOB + MAN)</td>
<td>£823</td>
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<td></td>
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<td></td>
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<td></td>
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<td>Cost per unit of outcome improved in:</td>
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<td>BGA versus SMT</td>
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<td></td>
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<td>Cost per QALY gained:</td>
<td>£17444</td>
<td>Recovery: £17,444</td>
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<td>PT</td>
<td>£1,174</td>
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<td></td>
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<td>Health effects</td>
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<td>£1,174</td>
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<tr>
<td></td>
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<td>-domination of SMT over GP care and PT in terms of recovery and pain</td>
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<tr>
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<td>Cost per unit of outcome improved in:</td>
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<td>Cost per QALY gained:</td>
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Table 4. (continued)

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<th>Study ID</th>
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<th>Health Outcomes</th>
<th>Mean Costs</th>
<th>Mean (SD) Health Effects</th>
<th>Difference in Costs</th>
<th>Incremental Ratio</th>
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<td>Lewis 2007</td>
<td>CUA, CEA</td>
<td>Disability (NPQ), EuroQoL</td>
<td>SMT (MOB + MAN) + A&amp;E</td>
<td>£367</td>
<td>Pain</td>
<td>Incremental costs: -£84</td>
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<td>Statistical analysis: Intention to Treat analysis, CIs for differences in means using parametric methods, CIs for uncertainty in cost estimates were based on bootstrapping (5000 simulations), linear regression to adjust for baseline covariates, multiple imputation technique to account for missing data</td>
<td>A&amp;E</td>
<td>Costs: £240</td>
<td>NPQ: 10.2 (14.1)</td>
<td>PSWD + A&amp;E (advice + exercise) - A&amp;E (advice + exercise)</td>
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<td></td>
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<td>A&amp;E care</td>
<td>£410</td>
<td>Health effects</td>
<td>Incremental costs: -£42</td>
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<td>A&amp;E</td>
<td>Costs: £240</td>
<td>NPQ: 10.3 (15.0)</td>
<td>PSWD + A&amp;E (advice + exercise) - A&amp;E (advice + exercise)</td>
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<td></td>
<td>A&amp;E</td>
<td>Costs: £240</td>
<td>QALY: 0.360 (0.094)</td>
<td>A&amp;E over SMT £65</td>
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<td>A&amp;E</td>
<td>Costs: £240</td>
<td>A&amp;E + exercise</td>
<td>Cost per QALY gained: A&amp;E over SMT £4672</td>
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<td>A&amp;E</td>
<td>Costs: £240</td>
<td>QALY: 0.362 (0.114)</td>
<td>A&amp;E over SMT £4672</td>
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<td>Shoulder Pain</td>
<td>CEA</td>
<td>Peceived recovery (%), shoulder pain, shoulder disability, general health</td>
<td>SMT (MOB + MAN) + GP care</td>
<td>£1443</td>
<td>Recovery: 41%</td>
<td>Incremental costs: £757</td>
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<td>Bergman 2010</td>
<td>Statistical analysis: paired sample t-test, bootstrapping (2000 replications) to compare mean costs between the groups and estimate 95% CIs, Intention to Treat analysis</td>
<td>A&amp;E</td>
<td>Costs: £1754</td>
<td>Pain: 5.9 (5.4)</td>
<td>General health: £25222</td>
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<td>Netherlands</td>
<td></td>
<td></td>
<td>A&amp;E</td>
<td>Costs: £1754</td>
<td>Disability: 33.0 (34.6)</td>
<td>General health: £25222</td>
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<td></td>
<td></td>
<td></td>
<td>A&amp;E</td>
<td>Costs: £1754</td>
<td>General health: 0.11 (0.19)</td>
<td>General health: £25222</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>A&amp;E</td>
<td>Costs: £1754</td>
<td>General health: 0.08 (0.21)</td>
<td>General health: £25222</td>
</tr>
<tr>
<td>Ankle Fracture</td>
<td>CUA</td>
<td>Quality of life (AQoL), activity limitation (LEFS)</td>
<td>MT + PT</td>
<td>£2267</td>
<td>Recovery: 41%</td>
<td>Incremental costs: £513</td>
</tr>
<tr>
<td>Lin 2008</td>
<td>Statistical analysis: Intention to Treat analysis, ANCOVA for group-differences, imputation of missing values, two sample t-test and bootstrapping (1000 replications) 95% CIs for group-differences in costs</td>
<td>PT</td>
<td>Costs: £1754</td>
<td>Pain: 5.2 (5.5)</td>
<td>Incremental effects: between-group difference AQoL: 1.3 (0.1, 2.5)</td>
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<td>Australia</td>
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<td></td>
<td>PT</td>
<td>Costs: £1754</td>
<td>Disability: 20.3 (35.9)</td>
<td>QALY: -0.09 (-0.6, 0.4)</td>
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<td></td>
<td></td>
<td>PT</td>
<td>Costs: £1754</td>
<td>General health: 0.08 (0.21)</td>
<td>Cost per QALY gained: -£1075</td>
</tr>
</tbody>
</table>

AQoL, assessment of quality of life; BGA, behavioral graded activity; BPM, brief pain management; CEA, cost-effectiveness analysis; CI, confidence interval; CUA, cost-utility analysis; EQ-5D, European Quality of Life-5 Dimensions; GP, general practitioner; HRQoL, health-related quality of life; LEFS, lower extremity functional scale; MAN, manipulation; MOB, mobilization; MT, manual therapy; NDI, Neck Disability Score; NPQ, Northwick Park Neck Pain Questionnaire; NR, not reported; ODI, Oswestry Disability Index; OSM, osteopathic manual therapy; PT, physiotherapy; QALY, quality-adjusted life year; RMDQ, Roland-Morris Disability; SMT, spinal manual therapy; VAS, visual analogue scale.

a High risk of bias (≤ 5 items of the recommended criteria by the Cochrane
b Low risk of bias (≥ 6 items of the recommended criteria by the Cochrane Back Review Group were satisfied)
alone or A&E plus pulsed shortwave diathermy (PSWD), but only at WTP thresholds of less than £100. For QALYs, at £30 000 per QALY gained threshold, the probabilities for A&E alone, A&E plus manual therapy, and A&E plus PSWD were 30%, 44%, and 26%, respectively.

Shoulder Pain. The trial by Bergman et al.57–60 evaluated spinal manual therapy plus usual GP care (relative to usual GP care alone in patients with shoulder pain. At 6 months of follow-up, the manual therapy group incurred nonsignificantly higher total costs compared with the GP care alone group (mean difference, £757). The mean improvements in perceived recovery (5.0%), shoulder pain (0.7), and general health (0.03) were in favor of the manual therapy group, but the differences were not statistically significant. The mean shoulder disability score was the only outcome significantly favoring the manual therapy over GP care (12.7). The ICERs for the manual therapy plus GP care vs GP care alone for perceived recovery, pain, disability, and general health were £151, £1081, £60, and £25 222, respectively.

Ankle Fracture. Lin et al.67,68 compared manual therapy added to physiotherapy with physiotherapy in patients with ankle fractures. At 6 months of follow-up, the mean between-group differences in mean AQoL score (1.3, P = .04), lower extremity function (−1.0, P = .70), and QALYs gained (−0.09) were not statistically significant. Similarly, there was no difference in total health care costs between the study groups (£513).

Discussion

This review identified limited evidence indicating that manual therapy techniques (eg, osteopathic spinal manipulation, physiotherapy consisting of manipulation and mobilization techniques, and chiropractic manipulation), in addition to other treatments or alone, are more cost-effective than usual GP care (alone or with exercise), spinal stabilization, GP advice, advice to remain active, or brief pain management for improving low back pain and/or disability. Similarly, one study demonstrated that spinal manipulation in addition to GP care was more cost-effective than GP care alone in reducing shoulder pain and related disability. The extra costs needed for 1-unit improvement in low back or shoulder pain/disability score or 1 QALY gained were lower than the WTP thresholds reported across the studies.

The cost-effectiveness of manual therapy for improving neck pain, disability, and QALYs gained in comparison with other treatments was not consistent across the studies. For example, one trial demonstrated the domination of chiropractic manipulation over physiotherapy or GP care in improving neck pain and QALYs gained. In 2 other trials, either alternative intervention (behavioral graded activity) was more cost-effective than manual therapy or the probability for manual therapy being more cost-effective compared with advice plus exercise was too low.

The evidence regarding cost-effectiveness of manual therapy compared with physiotherapy for reducing pain and disability related to ankle fractures, as reported in one study, has been insufficient and inconclusive because of small sample size and uncertainty around the cost-effectiveness measure.

It is difficult to draw definitive conclusions regarding the comparative cost-effectiveness of manual therapy techniques in patients with spinal pain due to the paucity, clinical heterogeneity (eg, different techniques, wide variety of comparators), and study-related shortcomings (eg, small sample, short follow-up, high uncertainty in the estimates of ICERs) of the identified evidence. For example, the use of different manual therapy techniques (eg, manipulation, mobilization, and chiropractic care) in combination with other interventions (eg, physiotherapy, exercise, and GP care) leads to differential effectiveness profiles, thereby limiting the comparability of results across studies. The nonspecific or contextual effects (eg, intervention fidelity, placebo effect, practitioner’s experience) due to the complexity of interventions and lack of patient blinding may have biased the study results for subjective outcome measures such as pain, disability, and QOL. Because none of the studies used a sham/control arm, it is difficult to tease out the specific effects of treatment from patients’ differential expectation (or practitioner’s experience/skill set) across the study treatment arms.

All the included studies were trial-based economic evaluations. None of the studies used economic modeling to extrapolate beyond the trial data to look at the longer-term cost-effectiveness of the different interventions. Studies reporting cost-effectiveness acceptability curves (CEACs) used bootstrapping, none of the studies used simple one-way or multiway sensitivity analyses to check for uncertainty in any of the key cost factors, which may be driving the ICER.

Limitations and Strengths

The findings of this review are not directly comparable with those of other systematic reviews, given the differences in scope, research question, study inclusion/exclusion criteria, types of economic evaluation, and interventions. The findings of these reviews were either inconclusive because of the paucity and heterogeneity of the evidence for manual therapy or showed some cost-effectiveness of manual therapy over alternative treatments (eg, usual care and exercise).

The applicability of findings of the included studies, despite them being pragmatic, may be limited to only countries with similar health care system and considerations of utility (eg, calculations based on the same QOL instrument). The applicability may also be limited by the
differences in components of manual therapy interventions and short follow-ups of the studies.

The strengths of the current review include the reviewer’s use of systematic and independent strategies to minimize the ROB in searching, identifying, selecting, extracting, and appraising the primary studies. The search strategy was applied to multiple electronic databases and other sources such as references of relevant primary studies and systematic reviews. Also, this review summarized the evidence from studies that evaluated costs and effectiveness simultaneously through cost-effectiveness and/or CUAs by providing ICERs. As a limitation, this review included only RCT-based cost-effectiveness evaluations.

This paper provides a platform for further research into the cost-effectiveness of manual therapy for the management of musculoskeletal conditions. The findings underscore the paucity of good-quality published evidence on this issue. This is based on the small number of identified RCTs focus of which is rather limited (ie, nonspecific spinal pain). The insufficient evidence on cost-effectiveness may be explained by difficulties in obtaining cost data, lack of expertise in economic outcomes, and/or perceived societal discomfort with assigning monetary units to human health.32 Raising awareness among the chiropractic community about the importance of undertaking more high quality economic evaluations is needed.

Because several studies did not use QALYs as an outcome measure, this presents difficulty for decision makers if they wish to compare value for money across musculoskeletal conditions with other health conditions such as cancer and cardiovascular disease, in line with the cost-effectiveness thresholds set by NICE. Consideration of the competing demand/supply side issues of manual therapy and how these issues may vary across countries is needed. Furthermore, it is not clear whether the affordability of manual therapy in countries where the provision of such services fall outside publicly funded arrangements is likely to influence utilization; this raises questions about the generalizability of the current reported findings.

We recommend that future studies report unit cost calculation with costs broken down by each service to allow the judgment as to whether all relevant costs for a given perspective were considered and how the total costs were calculated. If ethically justifiable, future trials need to include sham or no treatment arm to allow the assessment and separation of nonspecific effects (eg, patient’s expectation) from treatment effects. More exploration is warranted about which characteristics of manual therapy (eg, mode/frequency of administration or choice of spinal regions) are important for clinically relevant and patient-centered outcomes. Finally, greater consideration is needed to improve reporting quality of primary studies evaluating manual therapy.

CONCLUSIONS

Preliminary evidence from this review shows some economic advantage of manual therapy relative to other interventions used for the management of musculoskeletal conditions. However, at present, there is a paucity of evidence on the cost-effectiveness and/or cost-utility evaluations for manual therapy interventions. Further improvements in the methodological conduct and reporting quality of economic evaluations of manual therapy are warranted in order to facilitate adequate evidence-based decisions among policy makers, health care practitioners, and patients.

**Practical Applications**

- There is some limited evidence indicating that manual therapy techniques are more cost-effective than usual GP care, spinal stabilization, GP advice, advice to remain active, or brief pain management for improving low back and shoulder pain/disability.
- The extra costs needed for 1-unit improvement in low back or shoulder pain/disability score or 1 QALY gained were lower than the WTP thresholds reported across the studies.
- The cost-effectiveness of manual therapy for improving neck pain, disability, and QALYs gained in comparison with other treatments was not consistent across the studies.

**FUNDING SOURCES AND POTENTIAL CONFLICTS OF INTEREST**

The project was funded by the Royal College of Chiropractors. No conflicts of interest were reported for this study.

**CONTRIBUTORSHIP INFORMATION**

Concept development (provided idea for the research): P.S.
Design (planned the methods to generate the results): A.T., C.C., R.C., P.S.
Supervision (provided oversight, responsible for organization and implementation, writing of the manuscript): P.S., A.C.
Data collection/processing (responsible for experiments, patient management, organization, or reporting data): C.C.
Analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): A.T., C.C., H.M.

Literature search (performed the literature search): A.T., C.C., R.C.

Writing (responsible for writing a substantive part of the manuscript): A.T., R.C., A.C., H.M., P.S.

Critical review (revised manuscript for intellectual content, this does not relate to spelling and grammar checking): A.T., C.C., H.M., P.S.

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2. Manipulation, Orthopedic/ 3196
3. Manipulation, Chiropractic/ 599
4. Manipulation, Spinal/ 947
5. Manipulation, Osteopathic/ 275
6. Chiropractic/ 2910
7. ((orthopaedic or orthopedic or chiropractic or chirotherapeutic or osteopathic or spine or spinal or vertebrale or craniosacral or cranial or cervical or lumbar or occipital or vertebral or thoracic or sacral or sacroiliac or joint) adj3 (manipulation or adjustment or mobilization or traction)).tw. 3748
8. ((manual or manipulation or mobilization) adj (therapy or intervention or treatment or rehabilitation)).tw. 2087
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 10834
10. Osteopathic Medicine/ 2395
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12. chiropractic.tw. 2684
13. chirotherapeutic.tw. 16
14. 10 or 11 or 12 or 13 6949
15. 9 or 14 14942
16. “friction massage”.tw. 22
17. naprapathy.tw. 13
18. Rolfing.tw. 17
19. “myofascial release”.tw. 53
20. “Bowen technique”.tw. 5
21. “apophyseal glide”.tw. 7
22. “bone setting”.tw. 47
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24. “body work”.tw. 103
25. “high-velocity low-amplitude”.tw. 94
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27. ((Maitland or Kaltenborn or Evjenth or Evje or Mulligan or McKenzie or Cyriax or Mills or Mennell or Stoddard) adj3 (manipulation or adjustment or mobilization or traction)).tw. 17
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48. english.ab. 34846
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53. editorial.pt. 282269
54. Animals/ 4854330
55. Humans/ 12014638
56. 54 and 55 1282233
57. 54 not 56 3572097

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58  51 or 52 or 53 or 57  
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97  exp "economics, hospital"/  
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99  economics, nursing/  
100  economics, pharmaceutical/  
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103  value for money.ti,ab.  
104  budget$.ti,ab.  
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108  ((energy or oxygen) adj expenditure).ti,ab.  
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117  Humans/  
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120  29 and 119  
121  93 or 120