Is multimodal care effective for the management of patients with soft tissue injuries of the shoulder? A systematic review of the literature

by

Rachel Goldgrub

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Abstract and Keywords

Shoulder injuries are common and cause significant pain and disability. Individuals who consult clinicians for shoulder pain are typically treated with multimodal care. However, little is known about the effectiveness of multimodal care. This systematic review examines the effectiveness of multimodal care for soft tissue shoulder injuries. Five databases were systematically searched, 5885 articles were screened, and 19 were critically appraised. The best-evidence synthesis includes ten high-quality RCTs. For subacromial impingement syndrome, multimodal care leads to similar outcomes as sham therapy, shock-wave therapy, corticosteroid injections and surgery. For rotator cuff tendinitis, a multimodal program (acupuncture, dietary advice, and enzyme tablets) is more effective than conventional care (supervised exercise, soft tissue therapy, manual therapy, and placebo tablets). For non-specific shoulder pain, multimodal care may be more effective than waitlist, but leads to similar outcomes as exercise or corticosteroid injections. Future research is needed to determine the effectiveness of multimodal care**.**

Key Words: shoulder impingement syndrome, shoulder pain, rotator cuff tendinitis, multimodal care, systematic review.

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Contents

List of Abbreviations

CI – Confidence interval

DASH – Disabilities of the Arm, Shoulder, and Hand Questionnaire

RCT – Randomized controlled trial

ITT – Intention-to-treat

MCID – Minimal clinically important differences

MYMOP – Measure Yourself Medical Outcome Profile

PEDro Scale - Physiotherapy Evidence Database Scale

PRESS – Peer Review of Electronic Search Strategies

PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RR – Relative risk

SIGN – Scottish Intercollegiate Guidelines Network

SF-36 – Short-form 36

SPADI – Shoulder Pain and Disability Questionnaire

Chapter One: Introduction

Shoulder pain is commonly caused by acute or repetitive injuries to muscles, tendons and ligaments (1). The shoulder girdle is one of the most complex structures of the body and is susceptible to various soft tissue injuries and inflammation that can cause minor to severe impairments (2). This can include grade I-III sprain/strains, tendonitis, subacromial impingement syndrome, bursitis, painful arc syndrome, adhesive capsulitis, and labral injuries.

In industrialized nations, shoulder pain affects 30.3% of adults (3, 4). According to the U.S. Department of Labor, work-related shoulder injuries are the most burdensome musculoskeletal injury and are associated with a median of 24 days off work (5). In Saskatchewan, Canada, workers with shoulder injuries who make a compensation claim take an average of 39 days off work (6).

Although it is a common reason to consult a general practitioner (GP), it is estimated that only half of patients with shoulder pain will seek care (7, 8). Shoulder pain is most commonly diagnosed as rotator cuff tendinopathy, subacromial impingement syndrome or biceps tendinosis (3, 9-13). Patients with musculoskeletal shoulder conditions frequently receive more than one diagnosis for their condition. Östör et al., 2005 (7) found 77% of patients with rotator cuff tendinopathy are also diagnosed with subacromial impingent syndrome, adhesive capsulitis, or acromioclavicular disease. This suggests that shoulder pain may involve multiple anatomical structures, or that the diagnoses may lack sensitivity and specificity.

In primary care clinics, patients with shoulder pain are primarily managed with multimodal care (14-18). Multimodal care involves at least two distinct therapeutic modalities provided by one or more health care professionals (14-18). However, randomized controlled trials (RCTs) commonly evaluate the effectiveness of single interventions, limiting their generalizability to

clinical practice (17). Thus, a divide may exist between research and clinical practice. This divide must be reconciled to guide clinical practice and provide the best available care to patients.

Previous systematic reviews have concluded that limited evidence supports the effectiveness of combining treatments for the management of shoulder injuries (19, 20). In 2003, Green et al. concluded that more trials are needed to examine the effectiveness of combining physiotherapy interventions (i.e. manual therapy, supervised/prescribed exercise, and electrotherapeutic modalities) (19). More recently in 2006, Trampas & Kitsios found limited evidence to support the effectiveness of combining manual therapy and exercise for the management of subacromial impingement syndrome (20). However, these systematic reviews are out-dated and included methodological limitations that restricted the validity of their conclusions. These limitations included pooling heterogeneous studies in meta-analysis and including studies with a high risk of bias in their synthesis.

The objective of my thesis is to conduct a systematic review to determine the effectiveness of multimodal care for the management of soft tissue injuries of the shoulder. Specifically, I aim to determine whether programs of multimodal care are effective compared to other interventions (single or multimodal), placebo/sham interventions or no intervention in improving self-rated recovery, functional recovery (e.g. return to activities of daily living, school and/or work), clinical outcomes (e.g. pain, disability, health-related quality of life, depression) and/or administrative outcomes (e.g. time to claim closure).

Chapter Two: Background

Anatomy

The shoulder girdle includes several anatomical structures: 1) the glenohumeral joint; 2) the acromioclavicular joint; 3) the sternoclavicular joint; and 4) the scapulothoracic joint (Figure I). These joints are supported by several ligaments (coracohumeral ligament, glenohumeral ligament, transverse humeral ligament), the rotator cuff muscles (supraspinatus, infraspinatus, teres minor, and subscapularis) and the muscles of the upper back and chest (serratus anterior, pectoralis minor, levator scapulae, trapezius, rhomboid major, and rhomboid minor) (21-23). Other anatomical components of the shoulder griddle consist of the articular capsule, glenoid labrum, and four bursae (23).

Epidemiology of Shoulder Injuries and Pain

1. Prevalence

According to a systematic review by Luime et al, the point prevalence of shoulder pain ranges from 7% to 27% in adults younger than 70 years and from 13.2% to 26% in those older than 70 years. In the same study, the authors reported that, in the general population, the one-month prevalence ranges from 19% to 31%; the annual prevalence from 5% to 47% and the lifetime prevalence from 7% to 67% (24).

The authors searched Medline, Embase and CINAHL from database inception to 2001using the following keywords: shoulder, glenohumeral, scapula, clavicular, acromion, rotator cuff, supraspinatus, supra-spinatus, infraspinatus, infra-spinatus, serratus anterior, subscapularis, not cancer, not animal, prevalence, and incidence. The inclusion criteria for the review were: 1) shoulder complaints; 2) cross-sectional study for prevalence or longitudinal study for incidence; and 3) adults (≥18 or older). Studies were excluded if: 1) the population suffered from a pathology (e.g. tumours, fractures, infections, inflammatory disorders, etc.); and 2) articles were

published in non-scientific journals. The methodological quality of relevant articles were independently assessed by three reviewers using a four-item quality checklist: 1) the sample was randomly selected from the population or the whole study population was approached and the sampling method was described; 2) the complaint, disorder or diagnosis was determined by predefined and reproducible criteria; 3) the measurement were valid and reliable and 4) the response rate was ≥ 60%.

Eighteen cross-sectional studies described the prevalence of shoulder pain. Overall, most studies: 1) randomly sampled participants (15/18); 2) clearly defined their criteria for a shoulder complain or disorder (15/18); 3) had a response rate ≥ 60% 13/15. However, only 2/15 studies used valid and reliable measurements (i.e. Nordic Questionnaire, visual analogue scales for pain, and the Shoulder Disability Questionnaire).

In their discussion, the authors hypothesized that the high variation in prevalence in due to the wide ranges of case-definitions used in the 18 studies.

2. Incidence

In their systematic review, Luime et al., (24) also reported that the annual incidence of shoulder pain in the general population ranges from 0.9% for adults aged 31 to 35 years, to 2.5% for those between the ages of 42 to 46 years, 1.1% for 56 to 60 years, and 1.6% for those between the ages of 70 to 74 years. These estimates were obtained from one study of randomly sampled adults from Stockholm, Sweden conducted between 1965 to 1968 (n= 4195) (25).

A more recent Swedish study measured the annual incidence of medically diagnosed shoulder conditions from a population-based health care registry from Skåne County (n=1,169,464) (26). The authors reported that, in 2006, the annual incidence of all shoulder conditions (diseases of

the musculoskeletal system and connective tissue) was 80 per 10 000 for women and 74 per 10 000 for men. The incidence of consultation for new onset shoulder pain increased with age for both men and women. In women, the incidence peaked between the ages of 50 – 59 years (129 per 10 000) and it peaked between the ages of 60 - 69 years in men (116 per 10 000) (26). Finally, in the U.K., in 2000, the cumulative incidence of general practitioner consultation for shoulder pain was 147 per 10 000. It was similar for men (145 per 10 000) and women (149 per 10 000) (27).

3. Factors associated with shoulder pain

I searched PubMed to identify systematic reviews and observational studies on the etiology of soft tissue shoulder injuries. Search limits for publication dates were set for 20 years.

Age

Evidence from two systematic reviews, and two cohort studies suggest that age is positively associated with shoulder pain (3, 24, 28, 29). Both reviews found that the prevalence of shoulder conditions peaked in older age (adults aged 70+) (24, 28). The cohort study found that the prevalence peaked slightly earlier (55 – 64 years) (3). Additionally, a study of the French working population found that age is positively associated with incident rotator cuff syndrome (29). The incidence peaked between the ages of 40-50 years (29).

Sex

Evidence from one cohort study, and one panel study found that women are associated with more shoulder pain than men (3, 30).

Occupational factors

Evidence from one systematic review, three cross-sectional designs, one cohort study, and one case-control study found that occupational factors may be positively associated with shoulder injuries/pain (29, 31-35). These factors included working with arms above shoulder level (29, 33-35), repetitive motions (29, 32, 34), lifting or carrying weight with either one hand or two (33-35), pushing/pulling weights (33-35), high perceived physical exertion (29, 32), posture (31, 35), and low support from either co-workers or superiors (29, 31, 33).

Smoking

Evidence from one systematic review, one cohort study, and one cross-sectional study suggest that current smoking is positively associated with shoulder pain (3, 36, 37).

Obesity

Evidence from one cohort study, one cross-sectional study, and one case-control suggest that body mass index (BMI) ≥ 30 is associated with shoulder pain (3, 36, 38). The cross-sectional study also suggest that a high waist-circumference (men ≥ 102.0 cm, women ≥ 88.0 cm) and a high waist-to-hip ratio (men > 1.0, women > 0.9) may be associated with shoulder pain (36).

Diabetes

Evidence from one cross-sectional and one case-control study found that type 2 diabetes increases the odds of having shoulder pain (36, 38).

Physical exercise

Evidence from one cohort study suggest that people with sedentary lifestyle are more likely to experience shoulder pain than people with some level of activity (3). However, one cross-

sectional study did not find an association between all levels of physical activity and shoulder pain (36).

4. Course of Shoulder Pain

Two cohort studies assessed the persistence rate of rotator cuff syndrome (32) and rotator cuff tendinitis and shoulder symptoms (39) in working populations.

Bodin et al found that men with jobs that involved high repetitive tasks for four or more hours a day were less likely to recover (P=0.034) (32). Similarly, men with jobs that involved high perceived physical exertion at work were less likely to recover (P=0.019). Women with shoulder pain lasting more than one month during the preceding 12 months (P=0.006), women with elbow pain during the preceding 12 months (p=0.046) or elbow pain during the past seven days (P=0.029), and women with hand/wrist pain during the preceding 12 months (P=0.031) were all less likely to recover (32).

Silverstein et al found that the persistence of rotator cuff tendinitis at one year was 33.3% in the right shoulder and in the left shoulder in a working population (39). They also reported that the one-year recovery rate for right and left-sided rotator cuff tendinitis is 39.4% and 52.4% respectively.

Health Care Utilization for Shoulder Injuries

In the UK, 2.4% of the population visit a GP for shoulder complaints every year (40). In Australia, approximately 50% of patients with shoulder pain consult a GP and 95% of these patients receive physiotherapy and medical care (8, 11). Moreover, 12% of Australians who consult chiropractors report shoulder pain.

In Sweden, 19% of women and 23% of men consult their doctor for a second time three months after their initial diagnosis (26). Moreover, in the U.K. 17.1% of patients are referred to secondary or tertiary care within three months following the onset of initial symptoms (27). These patients consulted physiotherapists (63.9%), orthopaedic surgeons or rheumatologist (26.9%), or one of the following: pain clinics, referrals for imaging or X-ray, general surgical referral or complementary medicine (9.2%). Individuals between the ages of 40-59 received the highest referral rates; at the end of the three year period.

Specific Interventions for the Management of Soft Tissue Injuries of the Shoulder

Several studies focussed on specific interventions for the management of soft tissue injuries of the shoulder. The effectiveness of these interventions has been reviewed by the Ontario Protocol for Traffic Injury Management Collaboration (OPTIMa). The methodology used to conduct these reviews is described in detail in Chapter Four.

For subacromial impingement syndrome, the OPTIMa reviews found that: 1) low level therapy is more effective than placebo treatment or ultrasound in providing short term pain reduction (41); 2) home-based stretching and strengthening exercises for the rotator cuff and scapular muscles are effective compared to no treatment (42); and 3) clinic-based progressive shoulder strengthening exercises are effective when compared to a wait list (42). These reviews also report that: 1) adding neck mobilization to a multimodal shoulder treatment does not provide any added benefits (43); 2) pre-tensioned tape and shockwave therapy are not effective compared to placebo (41); and 3) local microwave diathermy and subacromial corticosteroid injections lead to similar outcomes (41).

For nonspecific shoulder pain, the OPTIMa reviews found that: 1) adding spinal manual therapy to usual care improved self-perceived recovery compared to usual care alone (43); 2) ultrasound and interferential current therapy are not more effective than placebo (41); and 3) supervised strengthening and stretching exercises, a corticosteroid injection, and a multimodal program of care lead to similar short-term outcomes (42);

Lastly, for persistent calcific tendinitis, shock wave therapy is more effective than sham treatment in reduction of short and long term shoulder pain and disability (41). The systematic review to determine the effectiveness of structured patient education did not find any relevant articles on soft tissue shoulder injuries (44).

However, the results of these studies may not be directly transferable to clinical practice because they focussed on single interventions (17). According to health care practitioners single interventions do not represent the "usual" clinical practice or the "most effective" care (45, 46). Hence, there is a need for a systematic review that determines the effectiveness of multimodal care for the management of soft tissue injuries of the shoulder.

Multimodal Treatment

In this review, multimodal refers to treatment involving at least two distinct therapeutic modalities, provided by one or more health care disciplines (14-16). A multimodal program can incorporate passive physical modalities, assistive devices, exercise, manual therapy, acupuncture, education, psychological interventions, or soft tissue therapies. RCTs of multimodal interventions provide a practical view of care occurring in clinics (15, 16).

Chapter Three: Literature Review

Scoping Search

A scoping search of the literature was conducted to review the existing systematic reviews on the effectiveness of multimodal care for the management of shoulder injuries. The aim of the scoping search was to determine the key concepts of the research area of interest and to evaluate the types of evidence that is available (47).

The following databases were searched: PubMed, Google Scholar and the Health Sciences databases available from the University of Ontario Institute of Technology library search (BMJ Journals, CINAHL, EBM Reviews, Health Source, MEDLINE, Nursing Reference Centre, ProQuest Nursing and Allied Health Source, PubMed, and SportsDisucus) from January 1st, 1990 to January 6th, 2014. Relevant reviews were critically appraised using the Scottish Intercollegiate Guidelines Network (SIGN) criteria for Systematic Reviews and Meta-analyses (Appendix II). The SIGN criteria helps make informed overall judgement of the risk of bias present in the reviews by assessing 11 methodological criteria: 1) clarity of the research question; 2) data selection and extraction; 3) comprehensiveness of literature search; 4) limitation of publication type; 5) listing of included and excluded studies; 6) characteristics of included studies; 7) assessment and documentation of scientific quality of included studies; 8) appropriate assessment of scientific quality of included studies; 9) appropriate methods used to combine findings; 10) publication bias assessed; and 11) declaration of conflicts of interest (48). The lead author tabled the amount of bias within each review assessed by the SIGN criteria (Table 1).

Study Selection

The search identified six reviews (11, 19, 20, 49-51); however none of the reviews focussed specifically on the effectiveness of multimodal care for the management of soft tissue injuries of the shoulder.

Study Characteristics

All six systematic reviews focused on adults (11, 19, 20, 49-51). Three of the reviews studied shoulder pain (11, 19, 51), two addressed subacromial impingement syndrome (20, 50), and one investigated upper extremity disorders (49). One of the reviews aimed to determine the effectiveness of physiotherapy interventions alone or in combination (19), one addressed the effectiveness of exercise and manual therapy either alone or in combination (20), two studied chiropractic care (11, 49), one tried to determine the effectiveness of manual and manipulative therapy (51), and one addressed conservative interventions (i.e. exercise, anti-inflammatory drugs, manipulation, mobilizations, ultrasound, acupuncture, physiotherapy) (50).

Risk of Bias

All six reviews had a clear research question and carried out a comprehensive literature search (11, 19, 20, 49-51). Three reviews had at least two reviews selecting studies and extracting data (19, 20, 51); five limited their review by publication type (19, 20, 49-51); three included a list of included and excluded studies (19, 20, 50); four reviews provided characteristics of included studies (11, 19, 20, 50); five assessed and documented the scientific quality of the included studies (19, 20, 49-51); three appropriately assessed the scientific quality of included studies (19, 20, 51); two used appropriate methods to combine individual study findings (20, 50), and two reviews declared conflicts of interest (19, 51). None of the reviews assessed publication bias (11, 19, 20, 49, 51).

Summary of the Reviews

Review One: Green et al, 2003 (19)

The aim of the review was to determine the effectiveness of physiotherapy interventions compared to placebo, no treatment, other interventions for the management of shoulder pain/dysfunction lasting greater than three weeks (19). The investigators searched MEDLINE, EMBASE, CINAHL, and Science Citation Index from 1966 to June 2002. The following MeSH terms were used: shoulder pain, shoulder impingement syndrome, rotator cuff, bursitis, rehabilitation, physical therapy techniques, musculoskeletal manipulations, exercise, ultrasonography, interventional, and free words; shoulder, rotator cuff, bursitis, impingement, tendinitis, pain, rehabilitation, physiotherapy, physical therapy, manual, exercise, therapy, ultrasound, TNS, TENS, shockwave, electrotherapy, mobilization, clinical trial, random, single or double, blind, mask, and placebo.

The inclusion criteria included: 1) randomized or pseudo-randomized controlled trails; 2) trials in which group allocation was not concealed to outcome assessors would be included but marked; 3) studies in all languages; 4) adults > 16 years; 5) shoulder pain or shoulder disorder greater than three weeks duration; 6) studies comparing physiotherapy interventions to placebo, no treatment, another intervention, or other physiotherapy interventions; 7) studies measuring pain, range of motion, function/disability, quality of life, strength, return to work, participants' perception of overall effect, global preference, physicians' preference and adverse events. Studies that included trauma, systemic inflammatory conditions, post- and perioperative shoulder pain, and pain in shoulder due to neck pain or pain from other parts of the body were excluded.

The internal validity of the trails was assessed using criteria based on the Physiotherapy Evidence Database (PEDro) Scale (52). The critical appraisal focussed on the methods of

randomization, allocation, concealment, blinding, number lost to follow up and intention to treat analysis. Each trial was reviewed independently by two reviewers, with addition of a third reviewer if consensus between the two reviewers could not be met. The data were meta-analysed using Rev Man 4.1. Trials with results that were not normally distributed were not included in the meta-analysis (e.g. studies presented data in terms of medians and not means). These studies were still included and described in an additional table.

A total of 67 trials were identified in the search and 26 trials were included in the analysis. Fourteen studies compared a physiotherapy modality to placebo (laser, bipolar interferential current, ultrasound, pulsed electromagnetic field). Eight trials compared one physiotherapy modality to another, and seven trials compared injections to physiotherapy.

The authors reported that combining mobilization with exercise resulted in additional benefits compared to exercise alone for patients with rotator cuff disorders. Moreover, they found that corticosteroid injections were superior to physiotherapy.

Review Two: Trampas and Kitsios, 2006 (20)

Trampas and Kitsios aimed to determine the effectiveness of exercise and manual therapy for the treatment of subacromial impingement syndrome in working age adults (18-66 years old). The authors searched AMED, CINAHL, EMBASE and MEDLINE from 2003 to 2005. The MeSH terms that were used included shoulder pain, shoulder impingement syndrome, rotator cuff, bursitis, rehabilitation, physical therapy techniques, musculoskeletal manipulations, and exercise movement techniques. To be included, studies had to investigate the effectiveness of exercise therapy or manual therapy in the treatment of subacromial impingement syndrome (however, studies with non-specific shoulder pain that included a high number of patients with subacromial

impingement syndrome were also included). The outcomes of interest included pain, strength, range of movement, functional test, and self-perceived change. Only RCTs published in English were considered.

The quality of the RCTs was scored using the PEDro scale (52). The PEDro scale includes 11 items that assess internal validly (7/11), descriptive validity (2/11), and statistical validity (2/11). The authors ranked a trial as high quality if it met at least six of the 11 methodical criteria being met and scored at least 4/7 on the internal validity score. Moderate quality trials met at least 5/11 of the methodological criteria and met an internal validly score of $\geq$ 3/7. Low quality trials scored $\leq$ 5/11 on the methodological criteria and <3/7 on the internal validity score. Two examiners assessed the RCTs independently. A third reviewer was involved if the two reviewers could not come to a consensus.

Of the 302 retrieved citations, 297 did not meet the inclusion criteria and five RCTs were eligible for critical appraisal. The mean quality score of the included trials was 6.2 (range from 4 to 8). Of the five relevant RCTs, one high quality article focused on the effectiveness of multimodal care (exercises in combination with other conventional treatments). Based on this study, the authors concluded that multimodal care that includes mobilization and exercise may be effective for pain relief and functional improvements, however the evidence is limited.

Review Three: McHardy et al, 2008 (49)

This systematic review examined the scope, type, and quality of chiropractic care (i.e. soft tissues strategies, electrotherapeutic, manipulative techniques) for the treatment of upper extremity disorders. The following databases were systematically searched: CINAHL, MEDLINE, and MANTIS from database inception to December 2005. The search includes the

following MeSH term; chiropractic and free words; shoulder, elbow, wrist, hand, forearm, and arm, shoulder impingement syndrome, brachial plexus neuritis, shoulder pain, shoulder joint, shoulder fracture, and shoulder dislocation.

To be included, a study had to document a diagnosis (no mention of what was considered a diagnosis) and the use of a chiropractic intervention. Articles were excluded if: 1) there was referred pain; 2) patients needed surgery; 3) the condition was not amendable to treatment; or 4) patients had major pathologies. Articles published in non-peer-reviewed literature, grand rounds, conference proceedings, and discussion papers were excluded.

Clinical trials (RCTs, non-RCTs, time series, case-control) were critically appraised using the PEDro scale (52). The authors determined that any clinical trial with a rating of 9-10 was of excellent quality, 6-8 was good, 4-5 was fair and anything below a four was of poor methodological quality.

A total of 1672 citations were retrieved and 64 papers were critically appraised and captured in the review. The authors found 36 case reports (PEDro score: 0) and three clinical trials [two RCTs (PEDro score: 4, and 7), and one time series (PEDro score: 0)]. A total of 32/36 of the case reports on patients with shoulder injuries were given multimodal treatment and one of the RCTs compared two multimodal programs.

The review reported that the typical chiropractic management of upper extremity disorders (including shoulder pain) is multimodal and combines passive and active treatments. However, this conclusion is hypothetical and needs to be confirmed with a large cohort study. The review concluded that higher-level evidence from RCTs is needed to determine the effectiveness of

chiropractic treatment for upper extremity conditions but the low level evidence that does exist supports chiropractic care for treatment.

Review Four: Pribicevic et al, 2010 (11)

This systematic review aimed to determine whether manual therapy/chiropractic techniques are effective for the management of shoulder pain. Five electronic databases were searched: MEDLINE, CINAHL, MANTIS, Cochrane Musculoskeletal Group Trials Register and Cochrane Controlled Trials Registers from 1985 to an unspecified date. The following MeSH terms and free words were used to search the literature: chiropractic, shoulder pain and manipulative therapy. Chiropractic was also searched with MeSH terms for the shoulder that included various combinations of chiropractic/physiotherapy, shoulder pain, impingement or rotator cuff, shoulder instability, shoulder joint, treatment or rehabilitation exercises.

Articles included in the review met the following inclusion criteria: 1) title had "shoulder pain" or a specific diagnosis; 2) contained a detailed description of the treatment intervention; 3) treatment performed by a registered practitioner of chiropractic, physiotherapy or medicine; 4) treatment was typical of the profession and included manipulative trust technique; 5) treatments performed by a registered chiropractor; and 6) the study included outcome measures.

The quality of the articles was scored using the PEDro scale (52). Again, articles with a rating of 9-10 are of excellent quality, 6-8 are good, 4-5 are fair and anything below a four is of poor methodological quality.

A total of 913 citations were retrieved and 30 articles (22 case reports, four case series, four RCTs) were included. Only the RCTs were assessed with the PEDro scale (two RCTs scored 8/10, one scored 6/10, and one scored 5/10).

All articles incorporated a multimodal chiropractic treatment utilizing a wide range of modalities. It was concluded, that strong evidence exists to support chiropractic care for upper extremity conditions albeit from poor methodology studies. Therefore, recommendations could not be made.

Review Five: Nyberg et al, 2010 (50)

The review examined conservative treatment interventions (i.e. exercise, anti-inflammatory drugs, manipulation, mobilizations, ultrasound, acupuncture, physiotherapy) for the management of subacromial impingement syndrome. PubMed, CINAHL, and the Cochrane Library were systematically search from January 1999 to May 31st, 2010. The MeSH terms included: shoulder impingement syndrome, shoulder pain, rotator cuff, tendinopathy, bursitis, rehabilitation, exercise, exercise therapy, physical therapy modalities, acupuncture, acupuncture therapy, resistance training, electric stimulation therapy, laser therapy, low level laser therapy, intervention.

The inclusion criteria were: 1) article must be a RCT; 2) diagnosis of subacromial impingement syndrome and/or established signs and symptoms; 3) conservative treatment alone, or in combination with other conservative treatments; 4) comparison group was placebo, other interventions or no interventions; and 5) clinical outcomes measuring pain and/or function.

Relevant RCTs were assessed using the PEDro Scale (52). The authors included all RCTs in their analysis regardless of the quality score. (A score of eight to ten meant the RCT was of high quality, seven meant medium and six or lower meant the RCT was of low quality.) The evidence was graded according to The Swedish Council on Technology Assessment in Health Care (SBU). Evidence grade one meant that a conclusion was supported by at least two studies of

high quality; evidence grade two meant that a conclusion was supported by at least one study of high quality and two studies with medium quality; and evidence grade three meant that a conclusion was supported by at least two studies with medium quality or one high quality study.

A total of 786 citations were retrieved. Thirty-five articles were eligible for critical appraisal following screening of titles and abstracts and removal of duplicates. Of those, 20 RCTs were included in the review. The breakdown of methodological qualities is as follows: 9/10 (one study), 8/10 (seven studies), 7/10 (four studies), 6/10 (two studies), 5/10 (three studies), 4/10 (two studies) and 3/10 (one study).

Only one study investigated multimodal care - the authors compared an individualized rehabilitation program to a no treatment group (53). Based on this study, the authors concluded that multimodal care is more effective than no treatment to manage subacromial impingement syndrome.

Review Six: Brantingham et al, 2011 (51)

The aim of this review was to determine the effectiveness of manual therapy for shoulder pain and dysfunction. The following databases were systematically searched from January 1983 to July 7, 2010: CINAHL; PEDro; and Index to Chiropractic Literature. Search terms used included: shoulder and spinal adjustments, spinal manipulation, mobilization and peripheral diagnosis, and randomized clinical trials and/or randomized controlled trials. Other search terms used were manipulation and one of the following terms: chiropractic, osteopathic, orthopedic, musculoskeletal, physical therapies, and manual therapies. The inclusion criteria was based on the inclusion criteria from McHardy et al (described earlier) (49) and an older review from the lead author focusing on manipulative therapy for lower extremity conditions (54).

Relevant randomized controlled trials and clinical trials were appraised using the PEDro scale (52). Their rankings for the PEDro scale consisted of: 1) very high quality RCT with a very low risk of bias (score of 9-10); 2) high quality RCT with low risk of bias (score of 7-8); 3) moderate quality RCT with high risk of bias (score of 5-6); and 4) low or poor quality RCT with very high risk of bias (score of 1-3).

Relevant case series and case reports were assessed using the Whole System Research (WSR) Assessment (55). The WSR, an 11-point scale, was developed to evaluate the internal validity of complementary and alternative medicine (55). A low quality case series/report would score 0-3, a medium quality score is 4-7, and a high quality score is 8-11.

After ranking each study by PEDro or WSR, the evidence was given a score as level A, B, C or I (insufficient) based on system created Harbour & Miller, 2001 (48).

- Grade A means there was good evidence. (These studies had: 1) appropriate designs and sufficient strength to answer the question; 2) results are both clinically important and consistent with minor expectations at most; 3) results are free of significant doubts about generalizability, bias and design flaws; and/or 4) negative studies have sufficiently large sample sizes to have adequate statistical power.
- Grade B evidence means there is fair evidence from relevant studies. These studies had: 1) appropriate designs of sufficient strength, but with inconsistencies or minor doubts about generalizability, bias, design flaws, or adequacy of sample size; and/or 2) evidence solely from weaker designs, but confirmed in separate studies.

- Grade C evidence means there is limited evidence from studies/reviews. These studies had: 1) substantial uncertainty due to design flaws or adequacy of sample size; and/or 2) limited number of studies weak design for answering the question addressed.
- Grade I (insufficient) means no recommendation can be made because of insufficient or non-relevant evidence.

A total of 211 citations were retrieved and 35 articles (23 RCTs, five control trials, and seven single-group pre-test post-test designs, case series and/or case reports) were included in the review.

The review found level B evidence to support the evidence of manual therapy of the shoulder girdle combined with multimodal care or exercise therapy for treatment of rotator cuff injuries/disorders, shoulder complaints, dysfunction, disorders or pain. It was recommended that multimodal treatment is the most effect method for shoulder injuries.

Synthesis of Systematic Reviews

Overall, only three of these systematic reviews were deemed to be of high quality (19, 20, 50). Nevertheless, these reviews also had limitations. The review by Green et al (19) included studies with small sample sizes (smallest study included only had 14 participants, seven per treatment arm). Studies with small sample sizes are liable to Type II errors. Additionally, due to the clinical heterogeneity of the 26 trials, only a few RCTs could be combined into a meta-analysis. Moreover, the quality of the trial was not used to stratify the evidence synthesis.

The review by Trampas & Kitsios (20) also had limitations. The authors limited the scope of their search to only two years, noting that this review is an update to another review conducted by different researches (56). However, they did not combine their update with the results of the

previous review. Furthermore, out of the five RCTs only 2/5 studies found that the review had a low risk of bias.

Forty percent of the studies included in the Nyberg et al. (50) review were considered low quality. Moreover, the impact of transforming the PEDro scale rating into the SBU evidence grade may have decreased the reliability of their results.

A major limitation in all three of these systematic reviews is the high risk of bias associated with including case series and/or case reports in their best evidence synthesis (11, 49, 51). Case series and case reports provide low quality of evidence because they do not have a control/comparison group and liable to selection and confounding bias. With these study designs, it cannot be determined that an improvement in shoulder pain or function is due to the treatment alone or to the natural history.

Finally, all previously conducted reviews are outdated. Therefore, there is a lack of information on the effectiveness of multimodal care for treatment of soft tissue injuries of the shoulder. A new systematic review that focuses on studies with a low risk bias is needed. This thesis will address this gap.

Chapter Four: Manuscript

Is multimodal care effective for the management of patients with soft tissue injuries of the shoulder? A systematic review by the Ontario Protocol for Traffic Injury Management (OPTIMa) Collaboration

Introduction

Musculoskeletal shoulder pain is very common in the general population, each year 30.3% of adults in industrialized nations will experience shoulder pain (3, 4). According to the Department of Labor in the United States, shoulder injuries are the most burdensome musculoskeletal injury, with workers requiring a median of 24 days off (5). Similarly, injured workers with shoulder injuries who make a claim to the Workers Compensation Board of Saskatchewan are, on average, absent for 39 days (6). Although it is a common reason to consult a general practitioner (GP), it is estimated that only about half of patients with shoulder pain will seek care (7, 8). Furthermore, around 20% of patients will consult their doctor after three months of initial diagnosis (26).

Shoulder pain is most commonly diagnosed as rotator cuff tendinopathy, subacromial impingement syndrome or biceps tendinosis (3, 9-13). However, patients with musculoskeletal shoulder conditions frequently receive more than one diagnosis for their condition. Östör et al., 2005 (7) reported that 77% of patients with rotator cuff tendinopathy are also diagnosed with subacromial impingent syndrome, adhesive capsulitis, or acromioclavicular disease. This suggests that shoulder pain involves multiple anatomical structures or that the diagnoses lack sensitivity and specificity (7).

In primary care clinics, patients with shoulder pain are primarily managed with multimodal care (14-17). Multimodal care involves at least two distinct therapeutic modalities provided by one or more health care professionals (14-17). However, randomized controlled trials (RCTs) commonly evaluate the effectiveness of single interventions, limiting their generalizability to clinical practice (17). Thus, to guide clinical practice and provide the best available care to patients, it is fundamental to understand the effectiveness of multimodal care. Previous

systematic reviews have concluded that limited evidence supports the effectiveness of combining treatments for shoulder injuries (19, 20). In 2003, Green et al. concluded that more trials are needed to examine the effectiveness of combining physiotherapy interventions (i.e. manual therapy, supervised/prescribed exercise, and electrotherapeutic modalities) (19). More recently in 2006, Trampas & Kitsios found limited evidence to support the effectiveness of combining manual therapy and exercise for the management of subacromial impingement syndrome (20). However, these systematic reviews are now out-dated and included methodological limitations that restricted the validity of their conclusions. These limitations included pooling heterogeneous studies in meta-analysis and including studies with a high risk of bias in their synthesis.

The objective of our systematic review is to determine the effectiveness of multimodal care for the management of adults and/or children with soft tissue injuries of the shoulder. Specifically, we aim to determine if multimodal care is effective compared to other interventions (singular or multimodal), placebo/sham interventions or no intervention in improving self-rated recovery, functional recovery (e.g. return to activities of daily living, school and/or work), clinical outcomes (e.g. pain, disability, health-related quality of life, depression) and/or administrative outcomes (e.g. time to claim closure).

Methods

Registration

This review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on March 26th, 2014 (registration number: CRD42014009115).

Eligibility Criteria

Population: The target population was adults and children with soft tissue injuries of the shoulder. We considered Grade I-II sprains/strains, non-specific musculoskeletal shoulder pain, bursitis, subacromial impingement syndrome, shoulder tendinitis, tendinosis, tendinopathy, and other soft tissue injuries of the shoulder as informed by available evidence (57-59). We excluded studies on patients with major structural or pathological causes of shoulder pain (e.g. fracture, dislocation, infection, frozen shoulder, systemic disease or neoplasm).

Interventions: We restricted the inclusion of studies to those that investigated the effectiveness of multimodal care. Multimodal care refers to a conservative program of care that involves at least two distinct therapeutic modalities, provided by one or more healthcare disciplines (14-17). A multimodal program of care can incorporate passive physical modalities, exercise, manual therapy, acupuncture, education, psychological interventions, soft tissue therapies, or other conservative interventions (i.e. NSAIDS) as informed by available evidence. The interventions included in multimodal care are adjuncts to each other; therefore, the effect of one intervention cannot be isolated. For example, a study comparing range of motion exercise, ultrasound and manual therapy to oral analgesics and education cannot be used to determine the effectiveness of any of the specific interventions. Only studies examining the effectiveness of multimodal programs of care commenting on the effect of one intervention compared to the whole program of care were included for review.

Comparison Groups: We included studies that compared multimodal care to single non-invasive interventions, other types of multimodal care, placebo/sham interventions, no intervention, or invasive interventions.

Outcomes: Eligible studies had to include one of the following outcomes: 1) self-rated recovery (e.g., self-reported on Likert Scale, Measure Yourself Medical Outcomes Profile); 2) functional recovery (e.g. Constant-Murley Scale, Shoulder Pain and Disability Scale; return to activities of daily living, work or school); 3) disability (e.g., Disability of Arm, Shoulder and Hand, Shoulder Disability Questionnaire); 4) pain (Visual Analogue Scale, Numerical Rating Scale); 5) health-related quality of life (Assessment of Quality of Life, Euro QoL-five dimension self-report questionnaire); 6) psychological status (Fear-Avoidance Beliefs Questionnaire, Tampa scale for Kinesiophobia); or 7) adverse events.

Study characteristics: Eligible studies met the following inclusion criteria: 1) English language; 2) peer-reviewed; 3) randomized controlled trial (RCT), cohort study, or case-control studies; and 4) included an inception cohort of at least 30 participants per treatment arm for RCTs, or 100 participants per group for cohort studies (this threshold was used to limit the impact of type II error on the overall evidence synthesis) (60).

We excluded the following: 1) guidelines, letters, editorials, commentaries, unpublished manuscripts, dissertations, government reports, books/book chapters, conference proceedings, meeting abstracts, lectures and addresses, consensus development statements, guideline statements; 2) pilot studies, cross-sectional studies, case reports/series, qualitative studies, non-systematic/systematic reviews, clinical practice guidelines, biomechanical studies, laboratory studies, studies not reporting on methodology; and 3) cadaveric or animal studies. Grey literature was excluded as these studies tend to have smaller sample sizes, smaller treatment effects, and have poorer methodological quality than published trials (61).

Data sources and Searches

We developed a search strategy with a health sciences librarian (Appendix I). A second librarian independently reviewed the strategy for completeness and accuracy using the Peer Review of Electronic Search Strategies (PRESS) Checklist (62, 63). We systematically searched MEDLINE, EMBASE, CINAHL, PsycINFO, and Cochrane Central Register of Controlled Trials from January 1st, 1990 to January 28th, 2015. The search strategy was developed in MEDLINE through Ovid Technologies Inc., and modified with the controlled vocabulary (thesauri) used by other bibliographic databases. Search terms consisted of subject headings specific to each database (e.g. MeSH in MEDLINE) and free text words relevant to multimodal care and shoulder injuries. The search results were imported into a database using bibliographic management software (EndNote X6; Thomas Reuters, New York, 2012).

Study Selection

Random pairs of reviewers independently screened the articles following a two-phase methodology after receiving standardized training. In phase I, each pair of reviewers screened titles and abstracts for relevance using the inclusion and exclusion criteria. The reviewers reached consensus on article eligibility. Articles were classified as relevant, possibly relevant or irrelevant. In phase II, the same reviewers evaluated the full text of possibly relevant articles to make a final determination of eligibility. Any disagreement between reviewers was resolved by discussion between the reviewers. If consensus could not be reached, a third reviewer independently reviewed the article and met with the other two reviewers to reach consensus.

Quality Assessment and Data Extraction

Relevant studies were critically appraised independently by pairs of reviewers (pool of nine reviewers). We used the Scottish Intercollegiate Guidelines Network (SIGN) criteria to help

trained reviewers make informed judgement of the internal validity of relevant RCTs, cohort studies, and case-control studies (48). We did not use a cut-off score to determine the internal validity of studies (64). Rather, we used the SIGN criteria to make an informed overall judgment on the risk of bias present in studies by assessing ten methodological criteria: 1) clarity of the research question; 2) randomization method; 3) concealment of treatment allocation; 4) blinding of treatment and outcomes; 5) similarity of baseline characteristics between groups; 6) co-intervention and contamination; 7) validity and reliability of outcome measures; 8) attrition; 9) intention-to-treat (ITT) analysis; and 10) comparability of results across study sites (where applicable) (65-70). Reviewers met to reach consensus on the internal validity of studies. If consensus could not be reached, an independent third reviewer was used to resolve disagreements.

We contacted authors if additional information was needed to complete the critical appraisal. Studies with a low risk of bias were included in our synthesis (71). The lead author extracted data from studies with a low risk of bias and built evidence tables (Table 1). A second reviewer independently checked the extracted data. Disagreements were resolved through discussion. Additionally, a senior epidemiologist reviewed the accuracy of the extracted data by cross-checking the data with the original studies during the manuscript preparation stage.

Data Synthesis and Analysis

We conducted a qualitative synthesis according to principles of best evidence synthesis (71). Best evidence synthesis is based on the principle that only studies with a high internal validity (low risk of bias) are used to determine the effectiveness of an intervention. We determined the clinical importance of results using minimal clinically important differences (MCIDs) (72-74).

The MCID thresholds include: 18/100 on the Shoulder Pain and Disability Index (SPADI) (73); 10.5/100 on the Disabilities of the Arm, Shoulder, and Hand Questionnaire (DASH) (72-74); 1.4/10 cm on the Visual Analog Scale (VAS) (75); 1.1/10 on the Numerical Rating Scale (76); and 1.14/7 for Symptom 1 and 0.91/7 for Symptom 2 on the Measure Yourself Medical Outcome Profile (MYMOP) (28). The MCID values for the Shoulder Disability Questionnaire and the Constant-Murley Score are not known (77). We stratified our results by shoulder diagnosis and duration [i.e. recent (< three months), persistent (≥ three months) or variable (all durations included)]. Since the diagnosis of shoulder conditions may lack validity, we chose to aggregate these conditions together and report them in different sections: subacromial impingement syndrome, nonspecific shoulder pain, and rotator cuff tendinitis (7).

We computed the inter-reviewer agreement [kappa coefficient (k) with 95% confidence interval (CI)] for the screening of titles and abstracts (78). The inter-reviewer percentage agreement for independent critical appraisal of articles was also calculated.

Where data were available, the difference in mean change between treatment groups was calculated with 95% CI to quantify the effectiveness of interventions. The computation of the 95% CI was based on the assumption that the pre- and post-intervention outcomes were highly correlated (r=0.8) (79, 80).

Reporting

This systematic review complies with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (81).

Results

Study Selection

We screened 5885 titles and abstracts for eligibility, including four abstracts identified through other sources [three from other OPTIMa Collaboration systematic reviews; one from hand searching the reference list of a previous systematic review] (Figure 1). Of those, 78 were screened in phase II (full text screening) and 19 articles were critically appraised. The primary reasons for exclusion at full text screening were: 1) ineligible interventions (26/59); 2) ineligible study designs (13/59); and 3) small sample size (10/59) (Figure 1). Nineteen articles (15 studies) were eligible for critical appraisal (53, 82-99). Of those, ten studies (published in 12 articles) had a low risk of bias and were included in the best evidence synthesis (82-93).

The inter-rater agreement for the screening of titles and abstracts was k=0.91 (95% CI 0.82; 1.00). The percentage agreement for the independent critical appraisal of the RCTs trials was 73.3% (11/15). For the four RCTs where reviewers disagreed, consensus was reached through discussion (four different pairs).

We contacted the authors of two studies to obtain additional methodological information for completion of the critical appraisal (53, 97); neither responded.

Study Characteristics

All ten studies with a low risk of bias were RCTs reporting on adults (Table 2) (82-93). Three RCTs investigated participants with persistent subacromial impingement syndrome (82, 84, 85, 88, 89) and two addressed subacromial impingement syndrome of variable duration (91, 92). Two RCTs studied persistent non-specific shoulder pain (83, 86), two RCTs targeted participants with variable duration non-specific shoulder pain (87, 90), and one addressed rotator cuff tendinitis of variable duration (93).

Twelve different multimodal programs of care were tested in the ten RCTs (Table 3). Moreover, 11 specific interventions were included in the multimodal programs: acupuncture, dietary advice, education, exercise, manual therapy, medication, passive modalities, psychological interventions, and soft tissue therapy. Most multimodal programs of care (11/12 programs) included exercise (82-93).

Risk of Bias

The ten RCTs with low risk of bias had a clearly focused and appropriate research question, used a valid randomization method, blinded data collection, and performed an intention-to-treat analysis (Table 2) (82-93). Nine studies had adequate allocation concealment (9/10) (82-86, 88-93). The distribution of baseline characteristics between treatment arms was similar in 70% (7/10) of the RCTs (82-87, 90, 93). Only one RCT with baseline differences between treatment arms controlled for these differences in their analysis (88, 89). Co-interventions did not differ between treatment groups in four of the trials (82-85, 91). The follow-up rate was greater than 70% in all admissible studies and most studies (8/10) had a follow-up rate that was above 80% (82-90, 92). Nevertheless, the studies with a low risk of bias had limitations. Specifically, several studies used outcome measures of unknown validity or reliability and these findings were excluded from our evidence synthesis (86-89, 91).

The five studies with a high risk of bias had important methodological limitations that threatened their internal validity (Table 4) (53, 94-99). These limitations related to the unspecified randomization method or concealment of treatment allocation (94-96, 98, 99); the unknown blinding of outcome assessment (96); baseline differences between treatment groups (53, 96, 98, 99); reliability and validity of the outcome (50, 94-96, 98-100); not reporting on co-interventions

(53, 96-99); and low rates of attrition (94, 95, 97-99). One study did not describe if an intention-to-treat analysis was conducted (96).

Summary of Evidence for Soft Tissue Injuries of the Shoulder

Persistent Subacromial Impingement Syndrome

Evidence from three RCTs suggests that various multimodal care interventions lead to outcomes similar to sham ultrasound, radial extracorporeal shock-wave therapy or subacromial decompression surgery plus exercise for patients with persistent subacromial impingement syndrome (82, 84, 85, 88, 89). In the first trial, Bennell et al. randomized participants with a positive quick test for shoulder impingement to: 1) multimodal care by a physiotherapist (soft tissue massage, passive mobilization of the glenohumeral joint, scapular retraining, postural taping, spinal mobilization); or 2) sham ultrasound therapy by a physiotherapist (Table 3) (82). Multimodal care was associated with a statistically significant difference in total SPADI score compared to sham ultrasound [mean change difference SPADI: 7.1 (95% CI 0.3; 13.9)] at 22-weeks follow-up. However, this difference was not clinically important. No other statistically or clinically important differences between groups in primary or secondary outcomes were identified at the 11-week and 22-week follow-up.

In a second RCT, Engebretsen et al. compared supervised posture and endurance exercise, manual techniques to loosen tense muscles, home-based resistance (low load) exercises, and simple advice provided by a physical therapist to radial extracorporeal shock-wave therapy provided by a physiotherapist in patients with a positive Kennedy-Hawkins sign (Table 3) (84, 85). There were statistically significant differences in the SPADI at 12 and 18 weeks [mean change difference of 10.3 (95% CI 0.8; 19.8) and 8.4 (95% CI 0.6; 16.5), respectively] in favour

of multimodal care. However, these changes were not clinically important. No clinically or statistically significant differences between groups were found with primary outcomes neither at one-year follow-up nor with any of the secondary outcomes at any follow-up points.

In their RCT, Haahr et al. randomized patients diagnosed with subacromial impingement syndrome by a specialist (duration > six months) to multimodal care (heat application, cold application, soft tissue therapy, supervised exercises, home exercise program), or to subacromial decompression surgery (bursectomy with partial resection of the antero-inferior portion of the acromion and the coracoacromial ligament) followed by instructions to perform strengthening exercises (Table 3) (88, 89). The type of soft tissue therapy provided to patients in the multimodal group was not described. There were no statistically significant differences for any of the outcomes at any follow-up point.

Subacromial Impingement Syndrome of Variable Duration

Evidence from two RCTs suggests that multimodal care may be associated with greater benefits than corticosteroid injection(s) for the management of subacromial impingement syndrome of variable duration (Table 3) (91, 92). However, the effect sizes were small and were not clinically important in long term follow-up.

In the first trial by Johansson et al., participants with subacromial impingement syndrome were randomized to: 1) multimodal care (acupuncture, home exercise) by a physiotherapist; or 2): a subacromial corticosteroid injection (methylprednisolone and lidocaine) and advice to limit heavy arm activity by a general practitioner (91). A second corticosteroid injection was offered if symptoms persisted. Participants in the multimodal care group were more likely to report improvement or recovery at the six-month follow-up [Relative Risk (RR): 1.46; 95% CL: 1.03;

2.07] but not at the 12-month follow-up. The primary outcome, pain and shoulder function, was not included in our synthesis as we could not find information on the validity and reliability of the measurement tool. There were no statistically or clinically significant differences for all other outcomes at any follow-up point.

The second RCT by Rhon et al. recruited adults with unilateral shoulder pain (in the glenohumeral region) meeting diagnostic criteria for shoulder impingement syndrome (92). Patients were randomized to either receive: 1) multimodal care by a physiotherapist (joint mobilization, soft-tissue mobilization, manual stretches and contract-relax techniques, along with a home exercise program); or 2) a corticosteroid injection provided by a general practitioner. Patients in the corticosteroid injection group could receive up to three injections over the course of one year if symptoms did not improve with the initial injection (had to wait at least one month between injections). At each follow-up point (one month, three months, six months, and one year), there were statistically significant differences favouring the multimodal group in pain on a Numeric Pain Rating Scale (NPRS). However, only the three month follow-up was clinically important [mean difference: 1.30/10 (95% CI 0.33; 1.47)]. Patients in the multimodal care group were less likely to visit a primary care provider after initial care than the corticosteroid group [RR: 0.64 (95% CI 0.43; 0.95)].

Rotator Cuff Tendinitis of Variable Duration

Evidence from a one RCT suggests that dietary advice along with acupuncture led to superior outcomes compared to supervised passive, active-assisted and active range of motion exercises combined with soft tissue and manual therapy for the management of patients with rotator cuff tendinitis of greater than six weeks duration (93). Szczurko et al. randomized patients with

rotator cuff tendinitis (duration ≥ six weeks) to: 1) diet-based multimodal care provided by a naturopath (needle acupuncture at pre-specified points with manual stimulation, anti-inflammatory diet, and the enzyme supplement Phlogenzym); or 2) an exercise and manual therapy based multimodal care program by a naturopath (passive, active-assisted and active exercise, soft tissue and manual therapy, and placebo tablets) (93). The specific description of soft tissue and manual therapy was not provided. There were statistically significant and clinically important differences favouring the diet-based multimodal program of care in pain and disability at the 12-week follow-up [mean difference: 28.97/100 (95% CI 19.91; 38.03)]. Moreover, the diet-based multimodal care group reported greater improvements in health-related quality of life [mean difference: PSC: 5.29/100 (95% CI 3.00; 7.58); MSC: 9.51/100 (95% CI 6.86; 12.00)]. There were also statistically significant and clinically important improvements in the secondary outcome measuring patient perceived improvements.

Persistent Non-Specific Shoulder Pain

Evidence from one RCT suggests that multimodal care may lead to better outcomes than wait listing for the management of persistent non-specific shoulder pain (83). Evidence from another RCT suggests that a multimodal care that includes graded exercise and behavioural therapy is associated with improved self-rated recovery compared to guideline-based usual care by a GP (86).

In their RCT, Bron et al., compared: 1) a multimodal program of care [soft tissue therapy, heat and cold, exercise (supervised stretching and home relaxation), ergonomic advice, postural instructions] provided by a physical therapist; and 2) a three-month wait list followed by multimodal care for patients with persistent unilateral non-traumatic shoulder pain (83).

Participants randomized to multimodal care reported statistically significant but non-clinically important differences in physical function and symptoms [mean difference: 7.2/100 (95% CI 2.61; 11.79)]. In addition, patients in the multimodal group were more likely to report global improvement post-intervention (12 weeks) [RR: 3.82 (95% CI 1.46; 9.96)].

In a second trial, Geraets et al. randomized patients to: 1) multimodal care program containing graded exercise therapy and behavioural treatment program (including time contingency and operant conditioning) by a physiotherapist (Table 3); or 2) guideline-based usual care by GPs which included information, recommendations, pain-contingent medical or pharmaceutical therapy (86). At the one-year follow-up, the graded exercise therapy group reported better activity performance than the GP guideline-based group [mean difference: 9.2/100 (95% CI 1.2; 17.3)] (the clinical importance of this difference is not known). Moreover, patients who received multimodal care were more likely to report having recovered. However, there was no difference in reported shoulder disability or in the psychological outcomes. It is important to note that at baseline, the patients who received the graded exercise therapy reported low levels of psychological impairment, and therefore may not have been responsive to the behavioural treatment program that was offered alongside graded exercise therapy (86).

Non-Specific Shoulder Pain of Variable Duration

Evidence from two RCTs suggests that multimodal care, corticosteroid injection (one to two injections) and exercise alone lead to similar outcomes for the management of variable duration non-specific shoulder pain (87, 90). In a three-arm RCT, Ginn and Cohen randomized patients with mild shoulder pain (baseline median pain intensity: 1.8/10 on a 10 cm VAS) of more than one month duration (mean duration: 7.3 months) to: 1) multimodal care (interferential therapy,

ultrasound, heat, cold, passive joint mobilization, daily range-of-motion exercise) by a physical therapist; 2) exercise (supervised and home-based stretching and strengthening exercises) by a physical therapist; or 3) one corticosteroid injection (methylprednisolone) by a rheumatologist (87). There were no statistically significant between-group differences identified in primary or secondary outcomes post-intervention.

In the second RCT, Hay et al. randomized patients with non-specific shoulder pain to: 1) multimodal care (advice and instruction on pain relief, active shoulder exercises, home exercise program, ultrasound and manual therapy) provided by a physiotherapist; or 2) corticosteroid injection (methylprednisolone and lidocaine) and advice to avoid shoulder overuse provided by a GP (90). A second corticosteroid injection was offered if symptoms persisted. There was no statistically significant difference between groups in shoulder disability immediately post-intervention. However, participants receiving the corticosteroid injection were more likely to report complete recovery immediately following the six week intervention [RR: 0.33 (CI 95% 0.14; 0.79)]. Findings from the six-month follow-up were not included in our synthesis due to the high crossover rates.

Adverse Events

Five of the ten admissible RCTs reported on the occurrence of adverse events (82, 84, 85, 91-93). No trials reported serious adverse events. The rate of non-serious adverse events ranged from 3.8% (84, 85) to 31.0% (82). In Engebretsen et al. a total of two patients in the radial extracorporeal shock-wave therapy group experienced aggravation of symptoms (84, 85). In the trial by Bennell et al., patients mostly experienced a high rate of minor adverse events due to the short-term pain associated with exercise and minor skin irritation from the tape (82). The minor

events included pain, skin irritation, bruising, tiredness, aggravation of existing symptoms, loose stools, sedation, abdominal discomfort, diarrhea, flatulence, constipation, skin flushing, burning ears, and tingling sensations (82, 84, 85, 91-93).

Discussion

Summary of Evidence

Our systematic review examined the effectiveness of multimodal programs of care for the management of soft tissue injuries of the shoulder. The preponderance of evidence challenges the use of current and conventionally administered multimodal care for subacromial impingement syndrome, rotator cuff tendonitis and non-specific shoulder pain.

Subacromial Impingement Syndrome

We did not find evidence that multimodal care programs are more effective than sham ultrasound (82), radial extracorporeal shock-wave therapy (84, 85), or surgery followed with exercises (88, 89) for persistent subacromial impingement syndrome. In fact, the evidence suggests that multimodal care may not be superior to placebo interventions.

However, for subacromial impingement syndrome of variable duration, we found some evidence that multimodal programs of care may lead to short-term improvements in recovery (91) and may help with short-term and long-term pain (92) when compared to corticosteroid injections.

Rotator Cuff Tendinitis

We found promising evidence that a multimodal program of care that combines dietary advice and acupuncture may be effective for the management of rotator cuff tendinitis of variable duration (greater than six weeks duration) (93). This multimodal program warrants further

investigation. In particular, the effectiveness of Phlogenzym has been debated in the literature. Studies of the effectiveness of Phlogenzym compared to NSAIDs in patients with osteoarthritis of the knee and hip resulted in conflicting evidence (101-104). Moreover, results from a randomised controlled trial found Phlogenzym was similar to placebo for the treatment of patients with acute unilateral lateral ankle strain (105). Therefore, further studies are needed and are likely to affect the conclusions of existing reviews.

Non-Specific Shoulder Pain

The evidence included in our review suggests that multimodal care may provide small benefits compared to wait listing (83) or guideline-based usual care by general practitioners for the management of persistent nonspecific shoulder pain (86); however, multimodal care leads to similar outcomes as stretching and strengthening exercises (87) or corticosteroid injections (87, 90) for nonspecific shoulder pain. It is important to note that the multimodal programs of care included in our review are heterogeneous; therefore, their effectiveness cannot be generalized without a close examination of their structure and frequency of care delivery.

Previous Systematic Reviews

The results of our review add to the literature on the effectiveness of multimodal care for the management of soft tissue shoulder pain. Previously, Green et al. reported that a combination of electrotherapy and exercises was less effective than corticosteroid injections (maximum of three injections) for rotator cuff disease (19). This result differs from ours as we found that there were no clinically important differences between multimodal care and corticosteroid injections (maximum of two injections). The results of the review by Green et al. may be explained by their

combining of methodologically heterogenic studies, which could have biased the results of their review. Moreover, our review includes more recent trials.

In a second review, Trampas and Kitsios, reported there was limited evidence to support multimodal care (exercise and manual therapy) for the management of shoulder impingement syndrome (20). However, these results should be interpreted with caution as the studies included in this systematic review had a high risk of bias (factors such as small sample size and clinical heterogeneity reducing the number of studies in the meta-analysis).

Finally, a systematic review by Nyberg et al. reported that multimodal care (individualized physiotherapy rehabilitation program) was more effective than a control intervention (no therapy with advice to maintain normal actives of daily living) in reducing pain and function in patients with subacromial impingement syndrome (50). However, this conclusion was based on the results of a single RCT by Dickens et al. that was excluded from our review due to a high risk of bias. Methodological concerns with the study by Dickens et al. include minimal information provided regarding baseline characteristics (sex, age, and mean constant score) and a further issue was the differential drop-outs rates (53).

Strengths and Limitations

First, our systematic review used the SIGN criteria and PRISMA statements as a guide to increase the internal validity of this systematic review, minimize risk of bias, and ensure the clarity of reporting (65-70, 81). Second, the search strategy was developed with a health sciences librarian, and was reviewed by a second librarian for accuracy and completeness. The inclusion and exclusion criteria were clearly detailed. Article screening and critical appraisal were completed by independent reviewers using a standardized methodology. Any disagreement was

resolved through a consensus process to help minimize selection bias. Reviewers were trained to use a standardised critical appraisal tool in advance of this review. Additionally, our conclusions are based on the SIGN criteria for qualitative evaluation of study quality, rather than applying an arbitrary cut-off score. This helps to minimize the risk of bias associated with using low quality studies in our best-evidence synthesis (64, 71). Finally, the MCID for each of the outcomes in all the studies was searched for in the literature to determine if a difference was clinically important.

Our review has limitations. First, our search was limited to journal articles published in the English language. Relevant studies may have been excluded if published in another language. However, this is not anticipated to be a significant source of bias as the majority of large trials are available in English (106). Furthermore, other systematic reviews in conventional medicine have examined the impact of language restrictions and found this limit did not lead to biased results (106-109). Additionally, we used MCIDs that were accessible in the literature. There is a chance that these MCIDs were computed from populations different from those reported in the admissible RCTs in our review and may lack generalizability.

Clinical Implications

Our systematic review highlights the importance of assessing the usefulness of combining clinical interventions for the management of soft tissue injuries of the shoulder. We found little evidence that multimodal programs of care are more effective than single interventions. In our review, we found that 41.7% (5/12) of multimodal arms included treatments (taping, mobilization, ultrasound, and interferential therapy) that were ineffective. Therefore, the development of future multimodal programs of care should be based on combining interventions

with demonstrated effectiveness. The current evidence suggests that patients with variable duration shoulder pain should be managed with supervised strengthening or home-based strengthening and stretching (42). Whether the effectiveness of strengthening and stretching exercises would be augmented by other interventions remains unclear.

Conclusion

Multimodal care is commonly used in clinical settings for treating patients. We found little evidence to support the effectiveness of multimodal care for the management of subacromial impingement syndrome or non-specific shoulder pain. However, we did find evidence that dietary advice, acupuncture and enzyme tablets are effective for the management of variable duration rotator cuff tendinitis when compared to supervised exercise, manual and soft tissue therapy, and placebo tablets at 12 weeks. We also found that a multimodal program (soft tissue therapy, heat and cold, exercise (supervised stretching and home relaxation), ergonomic advice, postural instructions) for 12 weeks may be beneficial for non-specific shoulder pain (≥6 months duration) when compared to wait list. The benefits reported by both of these multimodal alternatives need to be replicated by other researchers before any conclusions can be made on their usefulness. Further research is needed to evaluate the effectiveness of multimodal care for the management of soft tissue injuries of the shoulder using valid and reliable outcome measures, and examining long-term follow-up.

Chapter Five: Final Discussion, Summary and Conclusions

Main Findings

The aim of this systematic review was to determine the effectiveness of multimodal programs of care for the management of soft tissue injuries of the shoulder. The available evidence suggests that the effectiveness of multimodal care for subacromial impingement syndrome, rotator cuff tendonitis and non-specific shoulder pain is not clearly established. In other words, it is not clear that combining interventions provides greater clinical benefits than using interventions on their own.

Subacromial Impingement Syndrome

The evidence shows that multimodal care programs are not superior to sham ultrasound (82), radial extracorporeal shock-wave therapy (84, 85), or surgery followed with exercises (88, 89) for the management of persistent subacromial impingement syndrome. However, for subacromial impingement syndrome of variable duration, we found evidence that multimodal programs of care may lead to short-term improvements in recovery (91) and may help with short-term and long-term pain (92) when compared to corticosteroid injections.

Rotator Cuff Tendinitis

We found evidence that a multimodal program of care that combines dietary advice, Phlogenzym and acupuncture may be effective for the management of rotator cuff tendinitis of variable duration (greater than six weeks duration) (93). This multimodal program warrants further investigation because the effectiveness of Phlogenzym has been debated in the literature. Studies of the effectiveness of Phlogenzym compared to NSAIDs in patients with osteoarthritis of the knee and hip resulted in conflicting evidence (101-104). Moreover, results from a randomized

controlled trial found Phlogenzym was similar to placebo for the treatment of patients with acute unilateral lateral ankle strain (105).

Non-Specific Shoulder Pain

The evidence suggests that multimodal care may provide small benefits compared to wait listing (83) or guideline-based usual care by general practitioners for the management of persistent nonspecific shoulder pain (86). However, multimodal care leads to similar outcomes as stretching and strengthening exercises (87) or corticosteroid injections (87, 90) for nonspecific shoulder pain. It is important to note that the multimodal programs of care included in our review are heterogeneous; therefore, their effectiveness cannot be generalized without a close examination of their structure and frequency of care delivery.

Previous Reviews

The scoping review conducted from January 1st 1990 to January 6th, 2014 identified six reviews (11, 19, 20, 49-51). None of these reviews focused solely on the effectiveness of multimodal care for the management of soft tissue injuries of the shoulder. The range of interventions included in these reviews ranged from shoulder pain (11, 19, 51), subacromial impingement syndrome (20, 50), and upper extremity disorders (49). The interventions addressed were physiotherapy interventions alone or in combinations (19), exercise and manual therapy (separately or in tangent) (20), chiropractic care (11, 49), manual and manipulative therapy (51), and conservative treatments (alone or combinations) (50).

Green et al. (19) reported that a multimodal program of care that includes mobilization and exercise was more effective than exercise alone for patients with rotator cuff disorders. However, this does not meet our definition of multimodal care since the added effects of mobilization can

be isolated. They also found that corticosteroid injections were superior to physiotherapy. Our review suggests otherwise; we found that multimodal care may be associated with greater benefits than corticosteroid injection(s) for the management of subacromial impingement syndrome (91, 92), and for nonspecific shoulder pain of variable durations we found that multimodal care is comparable to corticosteroid injections(s) (87, 90).

Trampas and Kitsios (20) found that multimodal care that includes mobilization and exercise may be effective for pain relief and functional improvement. This conclusion was based on one study that compared acupuncture with exercise to ultrasound with exercise (76). The authors describe this as multimodal care, however since the effects of acupuncture and ultrasound can be determined individually, it does not fit our definition.

Two reviews that focused on the effectiveness of chiropractic care reported that multimodal programs of care may be effective. However, this conclusion is not justified because both reviews used case series and case reports to support their claim (11, 49). Since these study designs do not have a comparison group, it cannot be determined that the improvements seen are from the treatment provided.

Brantingham et al. (51) found evidence that manipulative therapy combined with multimodal care or exercise therapy is effective for the treatment of soft tissue injuries of the shoulder. However, the authors also included case series and case reports into review. Additionally, they included RCTs and clinical trials with low scores on the PEDro scale (range: 4/10 – 9/10), and the majority of the RCTs included had small sample sizes.

Finally, a systematic review by Nyberg et al. (50) reported there was limited evidence that supports the use of multimodal care in reducing pain and function in patients with subacromial

impingement syndrome. However, this conclusion was based on the results of a single RCT by Dickens et al. that was excluded from our review due to a high risk of bias. Methodological concerns with the study by Dickens et al. include minimal information provided regarding baseline characteristics (sex, age, and mean constant score) and issue was the differential drop-outs rates (53).

Clinical, Policy and Insurance Implications

Limited evidence exists to support that multimodal programs of care is more effective than single interventions or placebo treatments for the management of soft tissue injuries of the shoulder. In our review, 41.7% (5/12) of the multimodal programs included treatments (taping, mobilization, ultrasound, and interferential therapy) that have been found to be ineffective. This is a major clinical issue as health care practitioners use multimodal care to treat patients (14-17). In the US, musculoskeletal injuries require workers to take a median of 24 days off work, and in Manitoba injured workers take an average of 29 days off work (5, 6). We need to develop programs of care that will help benefit these patients, and save costs. There are major expenses associated with these therapies, and this is a major concern for insurance boards. In publicly funded health care systems such as Canada, there is a need for evidence-based practice that can influence policy.

Future Research

Our systematic review highlights the importance of assessing the usefulness of combining clinical interventions for the management of soft tissue injuries of the shoulder. We found little evidence that multimodal programs of care are more effective than single interventions. In our review, we found that 41.7% (5/12) of multimodal arms included treatments (taping, mobilization, ultrasound, and interferential therapy) that were ineffective. Therefore, the

development of future multimodal programs of care should be based on combining interventions with demonstrated effectiveness. The current evidence suggests that patients with variable duration shoulder pain should be managed with supervised strengthening or home-based strengthening and stretching (42). Whether the effectiveness of strengthening and stretching exercises would be augmented by other interventions remains unclear.

Conclusion

In clinical settings, multimodal care is commonly used to treat patients. There is little evidence to support the effectiveness of multimodal care for the management of subacromial impingement syndrome or non-specific shoulder pain. Nonetheless, we did find evidence that dietary advice, acupuncture and enzyme tablets may be effective for the management of variable duration rotator cuff tendinitis when compared to supervised exercise, manual and soft tissue therapy, and placebo tablets at 12 weeks. We also found that a multimodal program (soft tissue therapy, heat and cold, exercise (supervised stretching and home relaxation), ergonomic advice, postural instructions) for 12 weeks may be beneficial for non-specific shoulder pain (≥ six months duration) when compared to wait list. The results of both of these studies need to be replicated by additional researchers before assumptions can be made on their effectiveness. More research is needed to evaluate the effectiveness of multimodal care for the management of soft tissue injuries of the shoulder using valid and reliable outcome measures, and examining long-term follow-up.

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Glossary

Acromioplasty	Removing part of the acromion to create more space for the rotator cuff
Acupuncture	Acupuncture interventions are defined in accordance with the World Health Organization as, body needling (traditional, medical, modern, dry needling, trigger point needling, etc.), moxibustion (burning of herbs), electroacupuncture, laser acupuncture, microsystem acupuncture (such as ear acupuncture), and acupressure (application of pressure at acupuncture points).
Adhesive capsulitis (frozen shoulder)	Condition which the shoulder capsule becomes stiff reducing motion and causes pain
Assessment of Quality of Life	The latter instrument encompasses 15 items covering five dimensions (illness, independent living, social relationships, physical senses, and psychological wellbeing). Item responses are all ordinal scales with four levels per item. Scores are scaled from−0.04 (worse than death) to 1.00 (perfect health).
Best evidence synthesis	Combination of the quantification of effect sizes and systematic study selection procedures of quantitative syntheses with the attention to individual studies and methodological and substantive issues typical of the best narrative reviews. Best-evidence syntheses focus on the "best evidence" in a field, the studies highest in internal and external validity, using well-specified and defended a priori inclusion criteria, and use effect size data as an adjunct to a full discussion of the literature being reviewed.
Biceps tendinosis	Inflammation or irritation of the upper biceps tendon(110)
Case-control study	Type of epidemiological observational study to determine if a outcome is sue to a certain exposure
Cohort study	Type of epidemiological observational study to determine is people without a disease will develop disease
Confidence interval	Range of values within the study samples parameter is estimated to fall within
Constant-Murley Scale	A 100-point scale with four subscales: pain, activities of daily living, strength, and range of motion. A higher score equates to higher functioning
Cost of illness study	Provide information about healthcare resources and costs allocated to different groups of patients
Disabilities of the Arm, Shoulder, and Hand Questionnaire	A 30-item (scored 1-5), self-report questionnaire that measures physical function and symptoms of several musculoskeletal disorders of the upper limb. A higher score equates to lower functioning
Dislocation, shoulder	When the humerus separates from the scapula at the glenohumeral joint
Education	Patient education is defined as a process of enabling individuals to make informed decisions about their personal health-related behaviour. For the purpose of the systematic review, we considered a patient education intervention to be a structured, standardized and condition-specific intervention. This intervention can be differentiated from the usual clinical education that is routinely provided by clinicians in the course of

	clinical care by its structured nature. We investigated structured education strategies that were delivered through pamphlets, books, videos, neck schools, discussion with healthcare providers, or the Internet, where the education intervention focused on reassurance or advice on activation, exercise, expected pain and its mechanism, prognosis, stress-coping skills, workplace ergonomics, self-care strategies or general health. We excluded education interventions that included supervised exercise or cognitive behavioural therapy
Euro QoL-five dimension self-report questionnaire	Descriptive system of health-related quality of life states consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression)
Exercise	Exercise is defined as any series of movements with the aim of training or developing the body by routine practice or as physical training to promote good physical health. We have chosen a broad definition of exercise therapy to be inclusive of a wide variety of techniques common in the treatment and rehabilitation of neck pain and whiplash-associated disorders. Exercise interventions could include any prescribed movements with the intent of affecting clinical outcomes with respect to neck pain and whiplash-associated disorders. We excluded studies where the intervention was advice or education only, for example, advice to engage in physical activity.
Fear-Avoidance Beliefs Questionnaire	Survey to predict patients with high pain avoidance behaviours. A higher score equates to more fear-avoidance behaviours.
Incidence rate	Number of new cases of a disease that occur during a specified period of time in a population at risk for developing the disease
Intention-to-treat (ITT)	Patients are analyzed in groups original assigned to.
kappa coefficient (k)	Measure of inter-rater agreement.
Lifetime prevalence	Proportion of the population that at some point in their life will be affected
Manual therapy	Manual therapy is defined as the application of hands-on and/or mechanically assisted treatments, including manipulation, mobilization and traction but excluding soft tissue therapy. Manipulation includes techniques incorporating a high velocity, low amplitude impulse or thrust applied at or near the end of a joint's passive range of motion (ROM). Mobilization includes techniques incorporating a low velocity and small or large amplitude oscillatory movement, within a joint's passive ROM. Traction is defined as a manual or mechanically assisted application of an intermittent or continuous distractive force.
Measure Yourself Medical Outcome Profile (MYMOP)	Patient-generated outcome questionnaire. Patients choose two task they would like to see improvement in
Minimal clinically important differences (MCID)	Smallest change that patient would classify as important
Multimodal care	Treatment involving at least two distinct therapeutic modalities,

	provided by one or more health care disciplines. The following were considered distinct therapeutic modalities: passive physical modalities and assistive devices; exercise; manual therapy which includes mobilization, manipulation or traction; acupuncture; education; psychological interventions; and soft tissue therapies. Examples: 1. Include treatment arms with the same intervention but provided by different health care disciplines. a. Treatment Arm 1: Manipulation and mobilization by physical therapist b. Treatment Arm 2: Manipulation and mobilization by chiropractor 2. Include treatment arms with different interventions provided by a single health care practitioner a. Treatment Arm 1: Supervised strengthening exercise plus spinal manipulation (physical therapist) b. Treatment Arm 2: Home exercise with advice (physical therapist)
Neoplasm	Abnormal growth of tissue
Non-steroidal anti-inflammatory drug (NSAID)	Common pain relievers that reduce inflammation and lower fevers
One-month prevalence	Proportion of the population that in one month will be affected.
One-year prevalence	Proportion of the population that in one year will be affected
Passive physical modalities	Various categories of passive physical modalities have been described previously. A passive physical modality is defined as a physical treatment involving a device that does not require active participation by the patient. For the purpose of the systematic review, passive physical modalities are divided into two categories: physico-chemical and structural. Physico-chemical modalities have a common intention to treat using either a thermal or electromagnetic effect: including cold, heat or light application affecting the body at the skin level, or light, ultrasonic or electromagnetic radiation affecting structures beneath the skin. Examples of passive applications to the skin surface include but are not limited to heat applications (hot packs/compresses/pads, hydrotherapy, fluidotherapy), and cryotherapy (cold packs, ice massage, vapocoolant spray). Examples of passive applications affecting structures beneath the skin surface include but are not limited to low level laser therapy (LLLT), electrotherapy (transcutaneous electrical stimulation (TENS), electrogalvanic stimulation (EGS), electrical muscle stimulation (EMS), microcurrent, pulsed electromagnetic therapy, ultrasound, microwave, and ultrasonic shockwave therapy. Structural modalities include non-functional assistive devices that may either encourage a state of rest in anatomic positions (e.g. pillows, seat cushions) or actively inhibit or prevent movement (e.g. collars, corsets, casts, slings, and rest splints). Functional assistive devices (e.g. shoe

	orthotics, tenodesis splints, taping, and assistive braces) may align, support or otherwise indirectly facilitate function in the affected region.
Point prevalence	Prevalence of the disease at a certain point in time
Primary care	Intended to meet the needs of most patients for medical treatment, care, preventive measures and rehabilitation
Psychological interventions	Psychological interventions consisted of psychological therapies including but not limited to behavioural or cognitive-behavioural therapy, interpersonal therapy, and relaxation or biofeedback. These interventions could either be led by a health care provider over one or more sessions, including in-person psychoeducation, or be delivered using a booklet/written material with a psychoeducation component, internet interventions or guided psychological self-help interventions.
Randomized controlled trial	Study where participants are randomly assigned to a treatment arm
Risk Ratio	A ratio of people affect to those who are not
Referred mechanical neck pain	Pain and tenderness of the lower neck and suprascapular area, referred to the shoulder and upper limb area; shoulder movement may be restricted. Movement of the cervical spine and shoulder may reproduce more generalised upper back, neck and shoulder pain.
Rotator cuff muscles	Network of four muscles (supraspinatus, infraspinatus, teres minor, subscapularis) that from a covering around the head of the humerus
Rotator cuff rupture	Tear within one or more of the rotator cuff tendons. Most common in the supraspinatus muscle and tendon.
Rotator Cuff Tendinopathy	Most common cause of shoulder pain, it offend occurs in the non-dominant arm and in non-manual workers. Wasting may be present on examination; active and resisted movements are painful and may be partially restricted, whereas passive movements are full, albeit painful. Painful arc is neither specific nor sensitive as a clinical sign, its presence reinforces the diagnosis of a rotator cuff disorder.
Short-form 36	A patient-reported survey that measures health status on 8 domains; vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, mental health
Shoulder capsule	Thin, loose sac that entirely envelops the joint and extends from the articular capsule and extends from the coracoid process of the scapula to the greater tubercle of the humerus
Shoulder girdle	Consists of the clavicle and the scapula that attach the upper limbs to the axial skeleton by a ligament system called the shoulder capsule, the rotator cuff muscles and the muscles of the upper back. The shoulder girdle forms an incomplete circle that allows for maximal flexibility of the upper limbs in all planes.
Shoulder Pain and Disability Index	Self-administered questionnaire that reports on two dimensions; pain and functional activates. A higher score equates to more pain and decrease functioning
Soft tissue injuries of the shoulder	The disorders that will be studied in this review include, but are not limited to, Grade I-II sprain/strains, nonspecific diffuse shoulder pain,

	shoulder tendonitis, impingement syndrome, bursitis of the shoulder, thoracic outlet syndrome, and other soft tissue conditions of the shoulder as informed by available evidence.
Soft tissue therapies	The definition of soft tissue therapy is based on the definition used by the Australian Acute Musculoskeletal Pain Guidelines Group. Soft tissue therapy is defined as a mechanical form of therapy where soft tissue structures are passively pressed and kneaded, using physical contact with the hand or mechanical device. Types of soft tissue therapy may include, but are not limited to, massage, deep-tissue therapy, friction massage, Swedish massage, myofascial release, trigger and pressure point therapy, shiatsu, tuina, reflexology, and craniosacral therapy. Joint mobilization, manipulation, traction, exercise, and soft tissue therapies using acupuncture points are excluded.
Sprain	A sprain involves a stretch and/or tear of a ligament that occurs when a ligament and/or joint is placed under excessive load. The severity of the sprain is graded according to the extent of ligamentous damage: • Grade 1 sprain: occurs when ligamentous fibres are stretched but remain structurally intact. • Grade 2 sprain: occurs when ligamentous fibres become partially torn. Physical stress reveals increased laxity with a definite end point. • Grade 3 sprain: occurs when a ligament is completely torn, leading to gross instability In the shoulder, sprains can occur in the supporting ligaments and capsule of the glenohumeral or acromioclavicular joints.
Strain	A strain involves injury to a muscle and/or tendon that occurs when the muscle is placed under a forcible stretch, either passively or during muscle contraction. The severity of the strain is graded according to the severity of muscle fibre damage: Grade 1 strain: occurs when less than 5% of muscle/tendon fibres are disrupted, with fascia remaining intact Grade 2 strain: occurs when muscle fibre/tendon discontinuity involves a moderate number of muscle fibres. Grade 3 strain: occurs when there is complete discontinuity in the muscle fibres In the shoulder, strains may involve the rotator cuff and supporting muscles of the glenohumeral and scapulothoracic articulation. Tendon strains involving the rotator cuff are often referred to as partial thickness tears (grade 1 and 2 strains) or full thickness tears (grade 3 strains). Shoulder impingement is commonly associated with sprain/strain injuries of the shoulder and occurs when the tendons of the rotator cuff become irritated as they pass beneath the acromion.
Subacromial bursitis	Acute or chronic inflammation of the subacromial bursa
Subacromial impingement syndrome	Inflammation and irritation of the tendons of the rotator cuff muscles as they pass through the subacromial space.

Appendix I: Figures

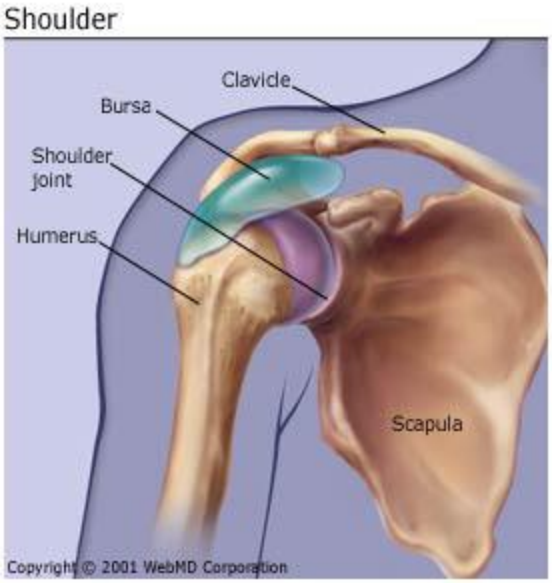

Figure 1: Illustration of the shoulder girdle **and** the following joints; the glenohumeral joint; the acromioclavicular joint; the sternoclavicular joint; and the scapulothoracic joint (thoracic ribs missing). (©2001, WebMD, LLC. All rights reserved)

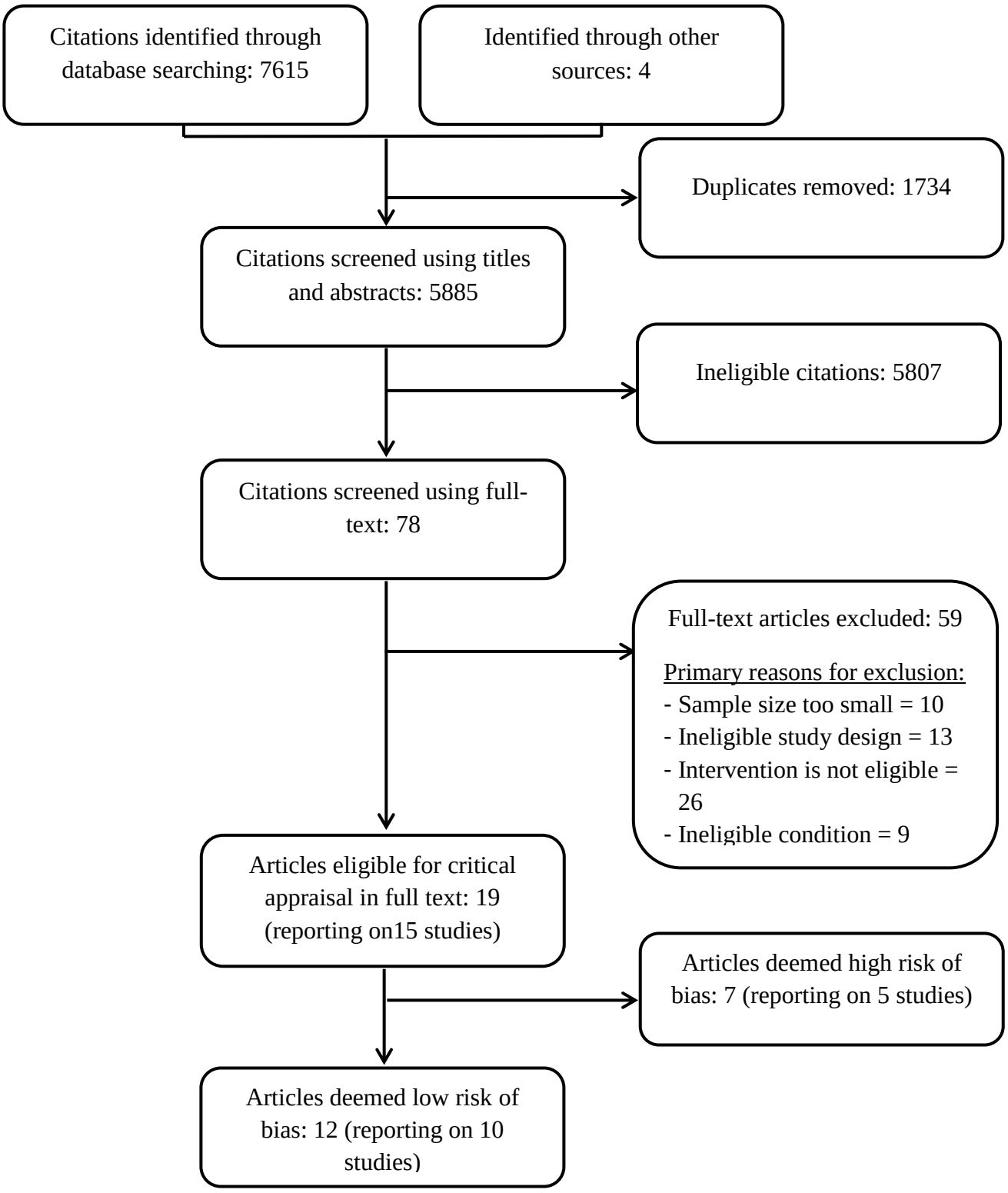

Figure 2: Identification and selection of articles

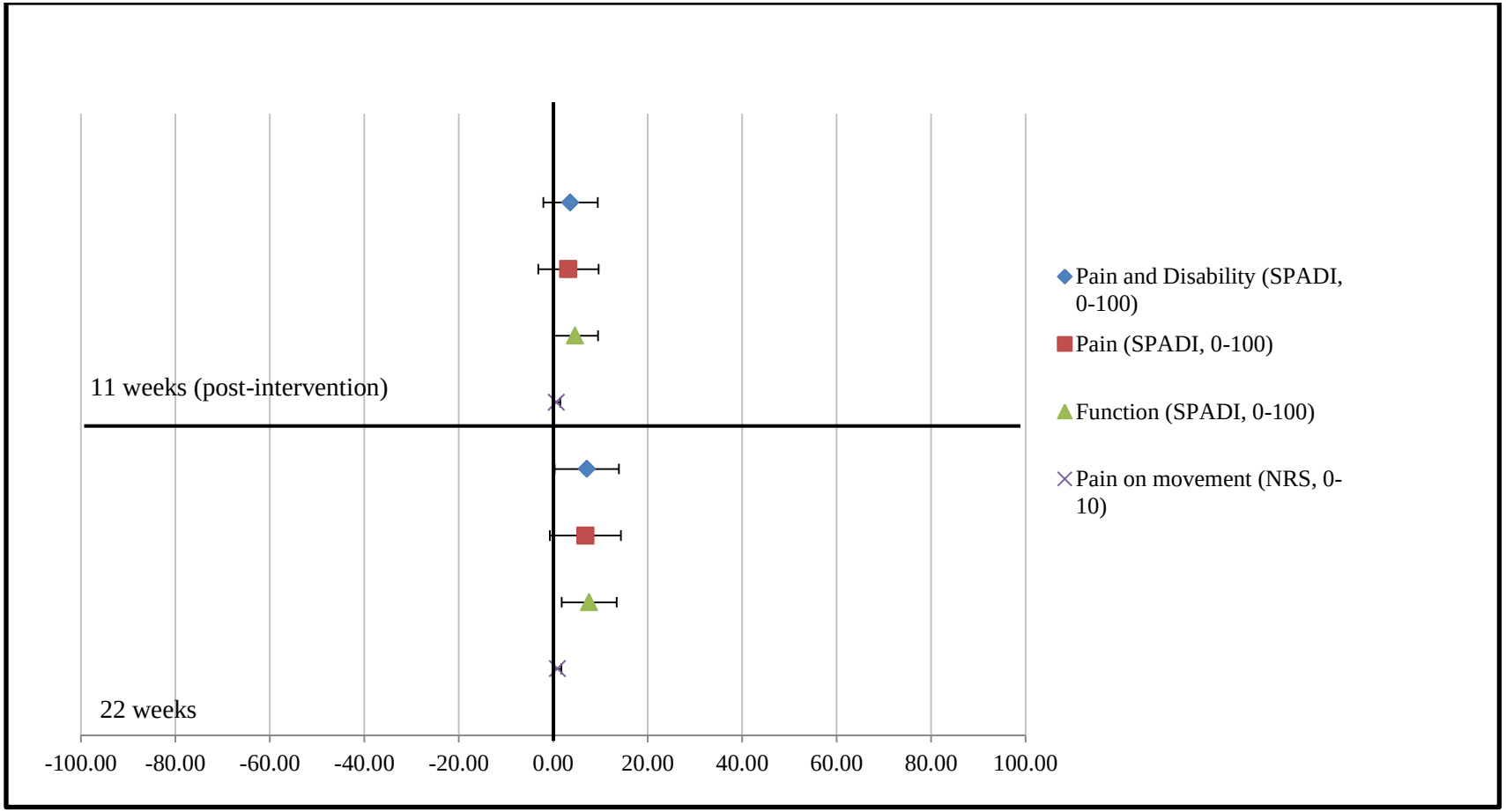

Figure 3: Difference in mean change in the primary outcomes between the multimodal care group and the placebo group in Bennell et al., (82) measuring shoulder pain and disability using the Shoulder Pain and Disability Index (SPADI), and pain on movement using a Numeric Rating Scale (NRS).

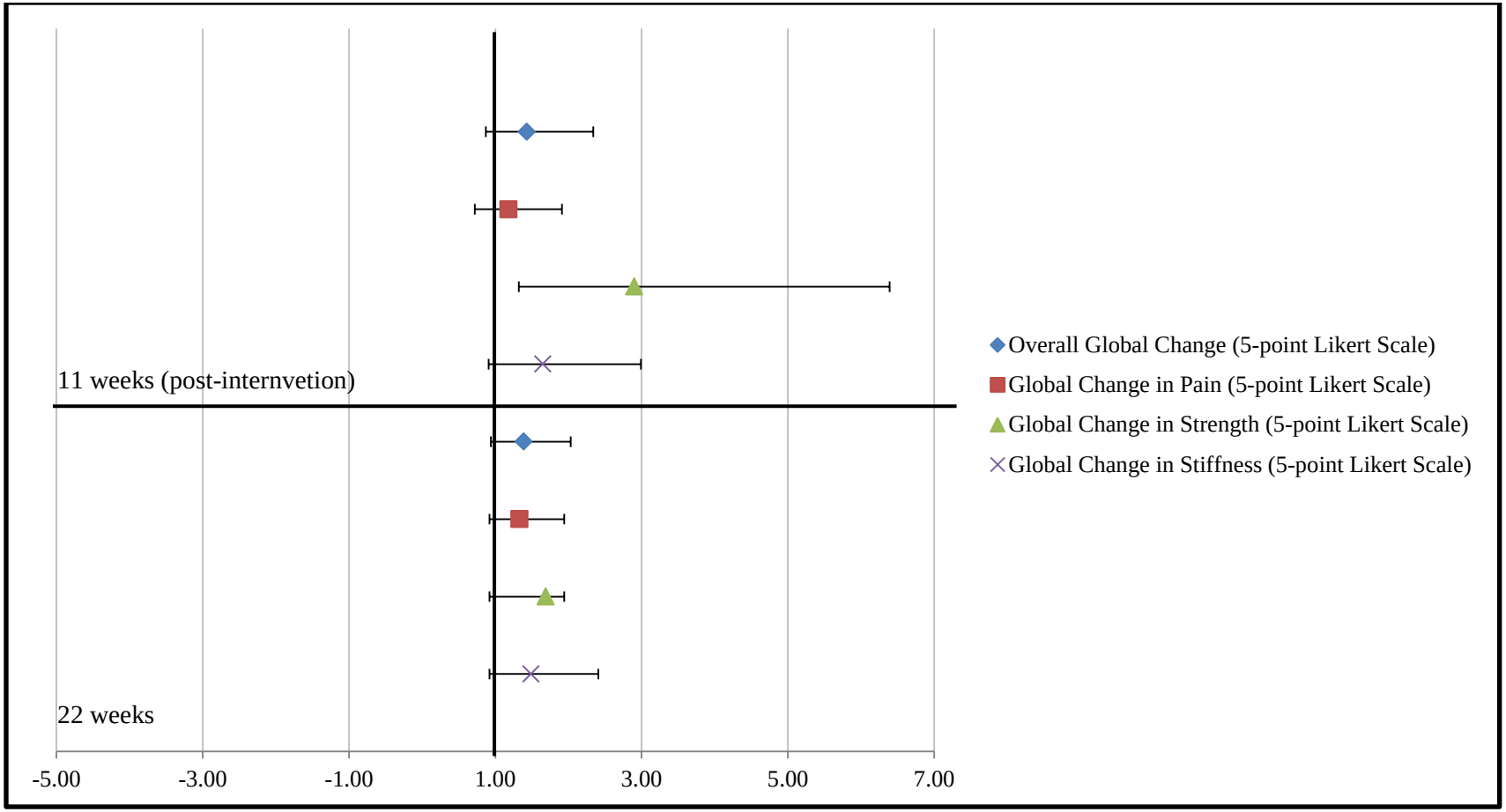

Figure 4: Relative risk of patients reporting a successful outcome (“much better”) between the multimodal care group and placebo group for the primary outcomes of overall global change, global change in pain, global change in strength and global change in stiffness (measured on a 5-point Likert Scale – “much worse”, “slightly worse”, “no change”, “slightly better”, or “much better”) (82).

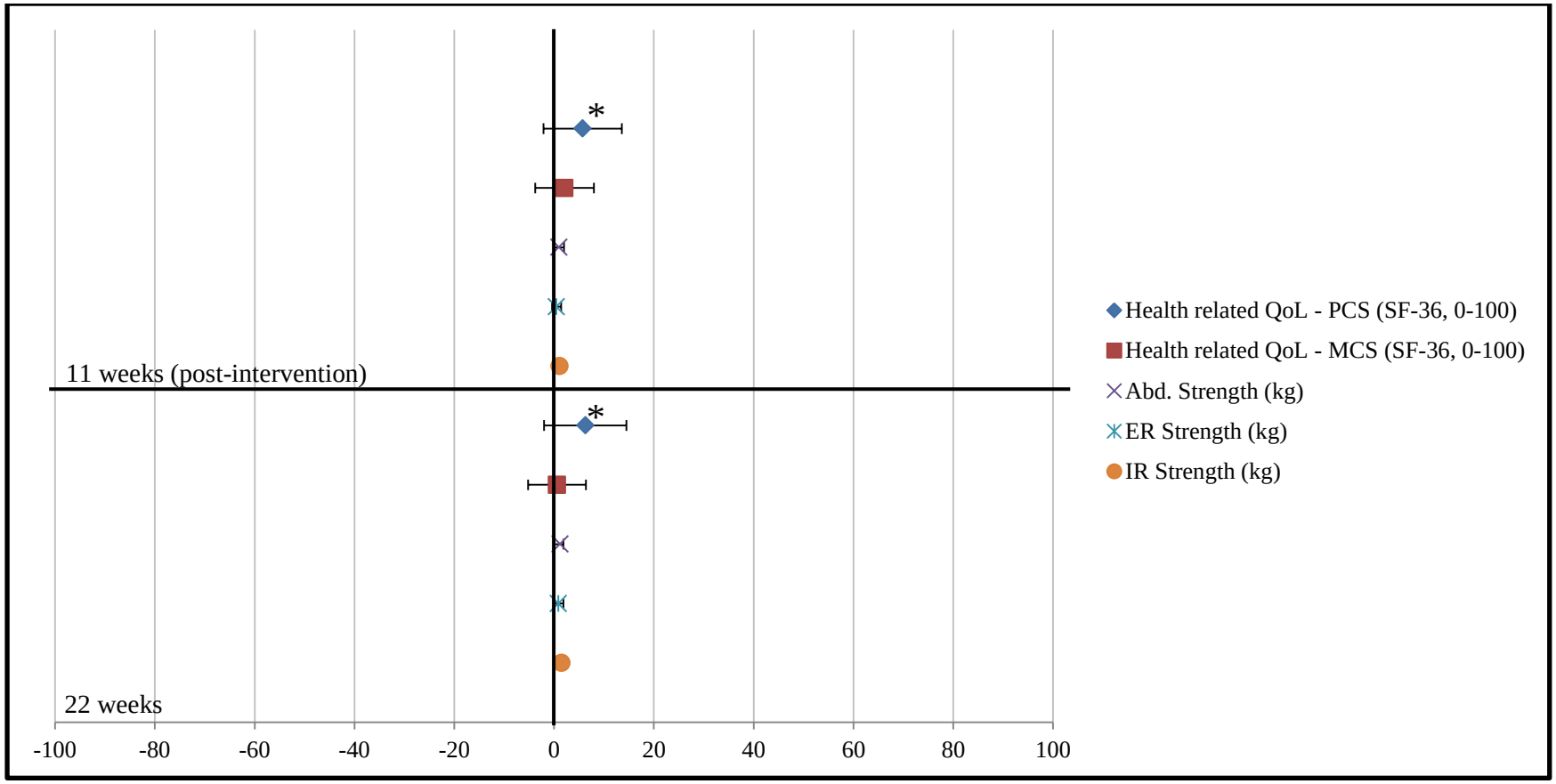

Figure 5: Difference in mean change between the multimodal care group for the secondary outcomes and the placebo group for quality of life (physical and mental) and strength (abduction, external rotation, and internal rotation) (82). (Legend: QoL: Quality of life; PCS: physical component scale; MCS: mental component scale; Abd: abduction; ER: external rotation; IR: internal rotation; kg: kilogram; *: clinically important)

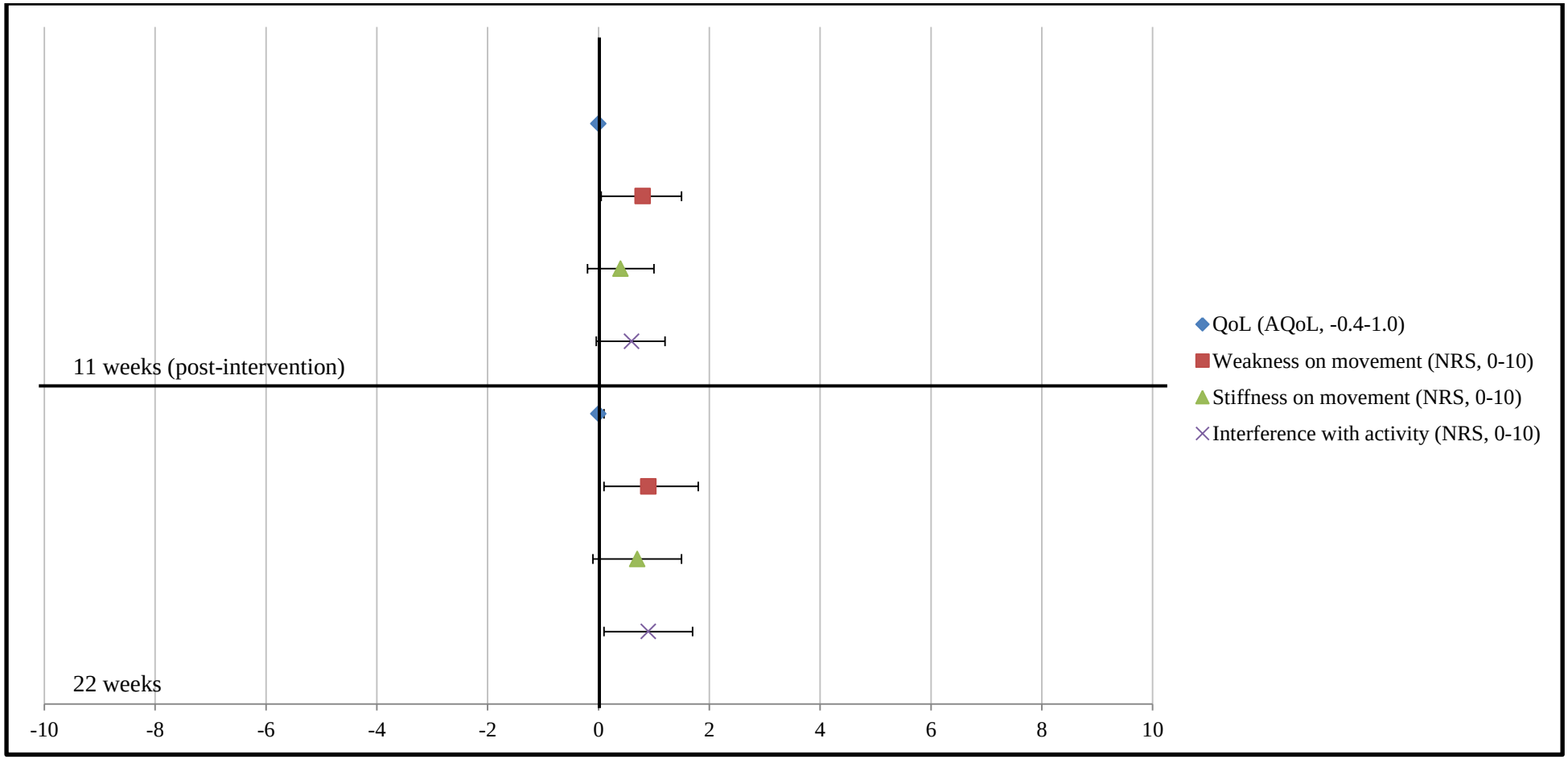

Figure 6: Difference in mean change between the multimodal care group for the secondary outcomes and the placebo for quality of life weakness on movement, stiffness on movement and interference with activity (82). (Legend: AQoL: Assessment Quality of life; NRS: Numeric Rating Scale)

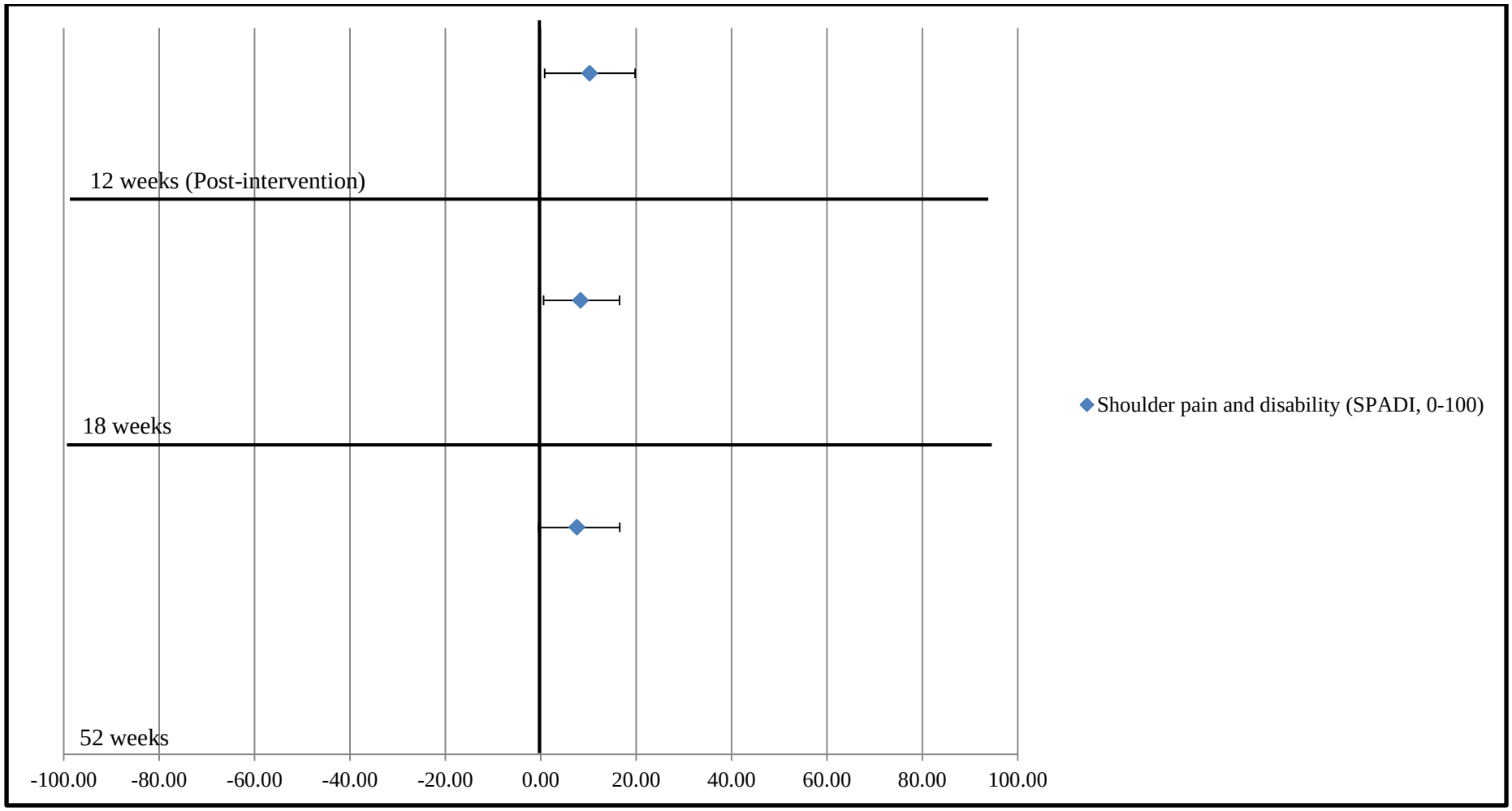

Figure 7: Difference in mean change in the primary outcomes between the multimodal care group and radial extracorporeal shock-wave therapy in Engebretsen et al., (84, 85) measuring shoulder pain and disability using the Shoulder Pain and Disability Index (SPADI).

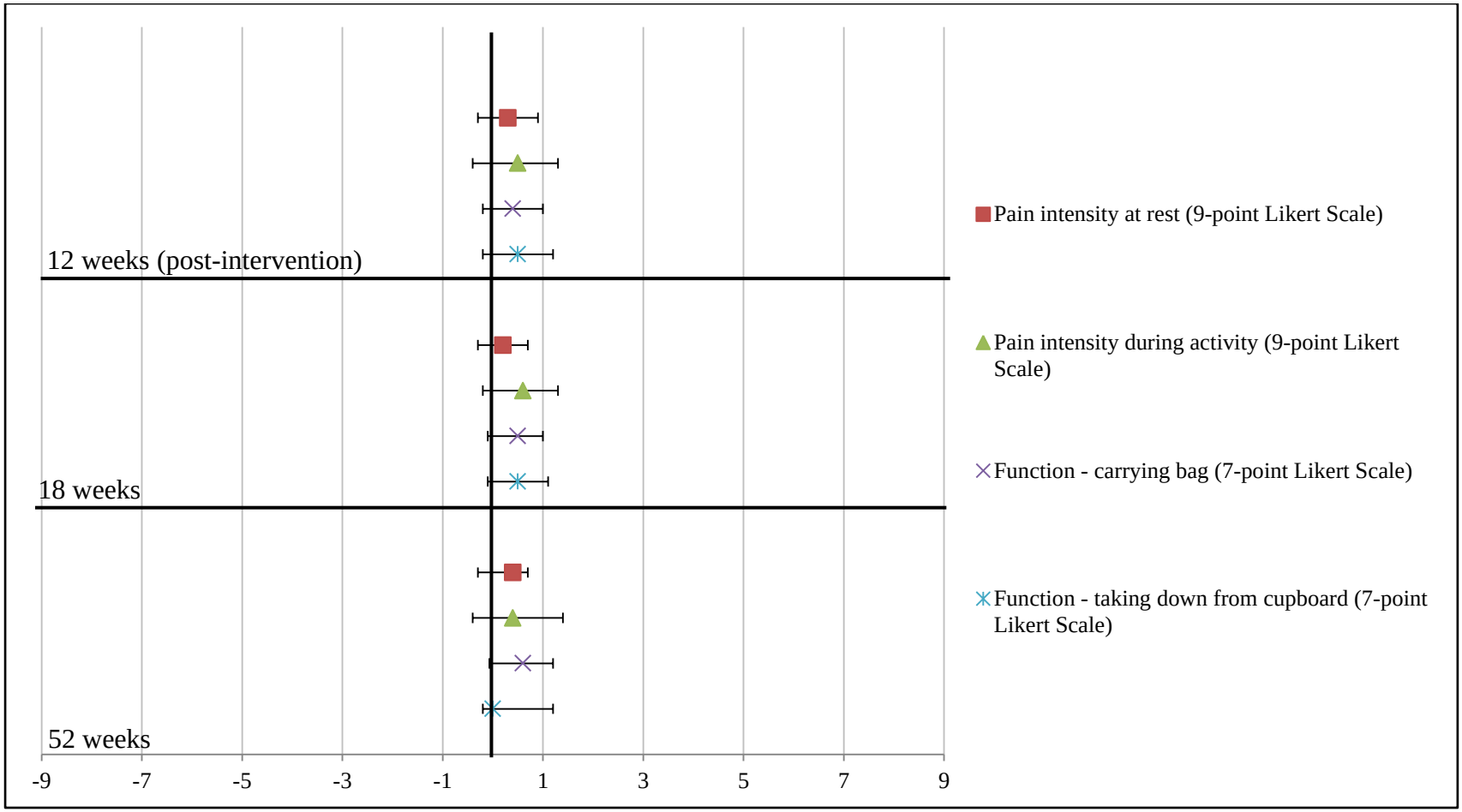

Figure 8: Difference in mean change in the primary outcomes between the multimodal care group and radial extracorporeal shock-wave therapy in Engebretsen et al., (84, 85) measuring pain intensity at rest, pain during activity using a 9-point Likert Scale (1=no pain; 9=severe pain) and functional task on a 7-point Likert Scale (1=easy; 7=impossible).

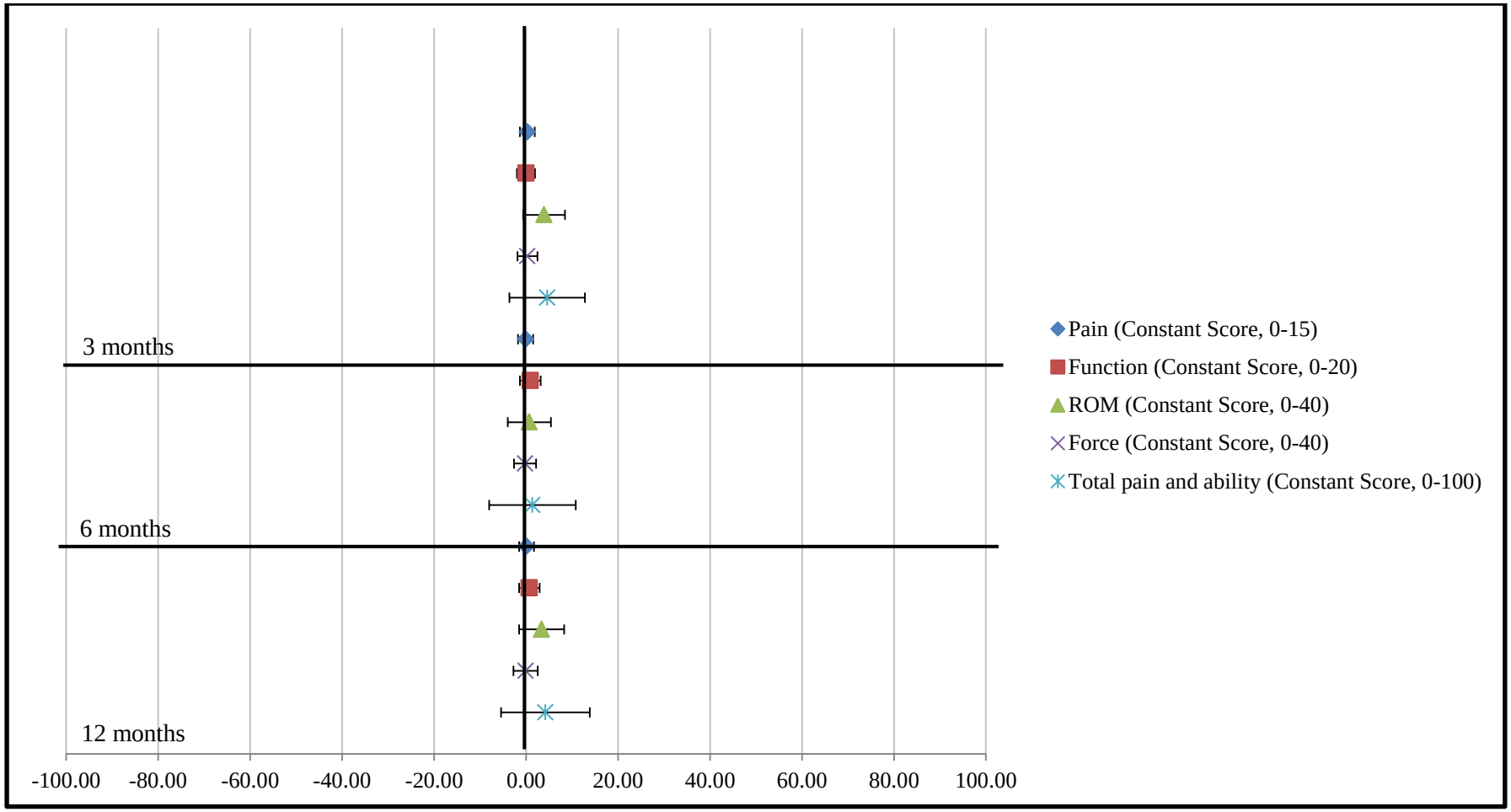

Figure 9: Difference in mean change between the multimodal care and subacromial decompression surgery in Haahr et al., (88, 89) measuring the total pain and ability using the Constant Score and the sub score of that scale. (Legend: ROM: range of motion)

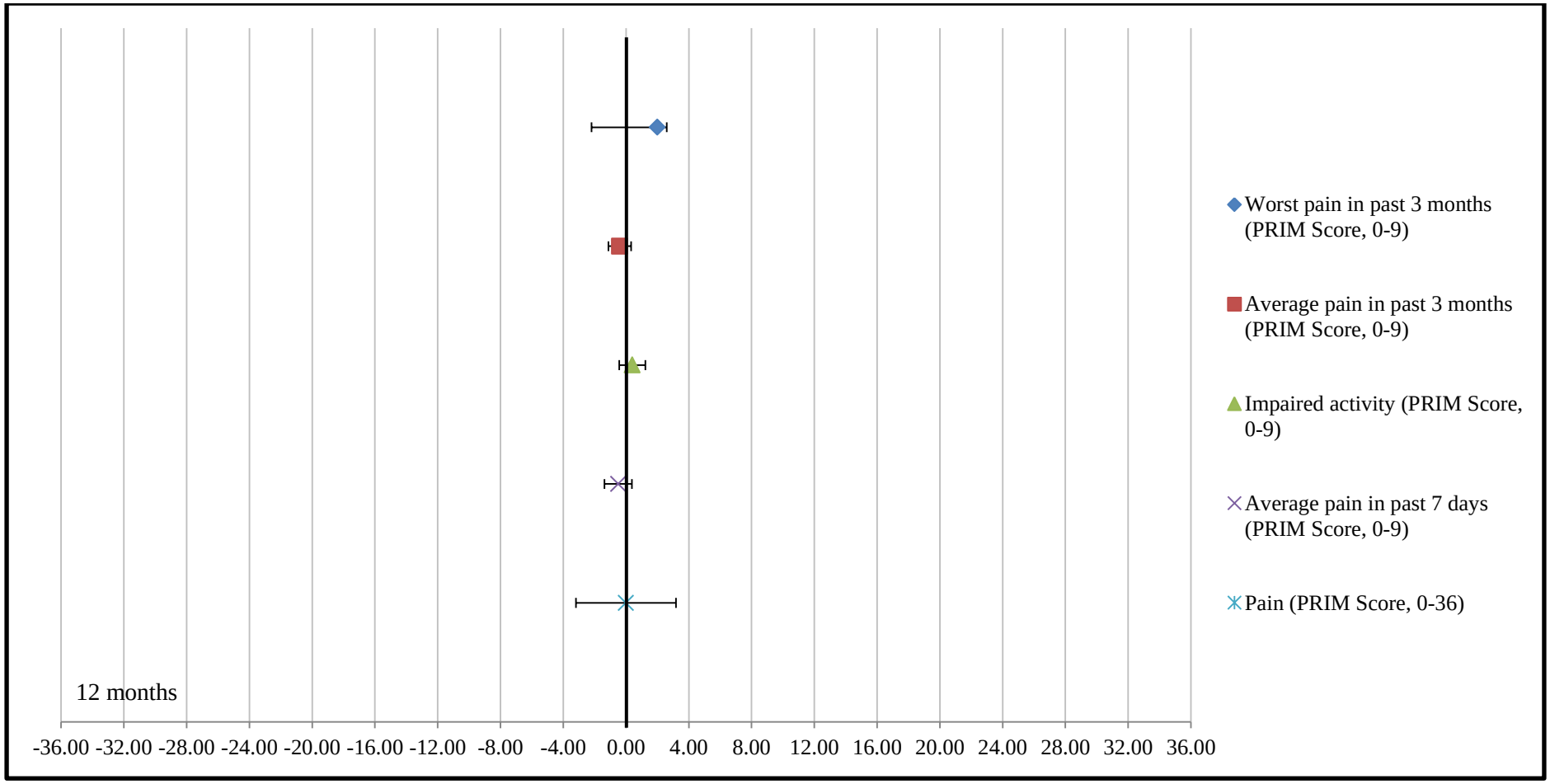

Figure 10: Difference in mean change between the multimodal care and subacromial decompression surgery in Haahr et al., (88, 89) measuring pain on the Project on Research an Intervention in Monotonous Work (PRIM) Score.

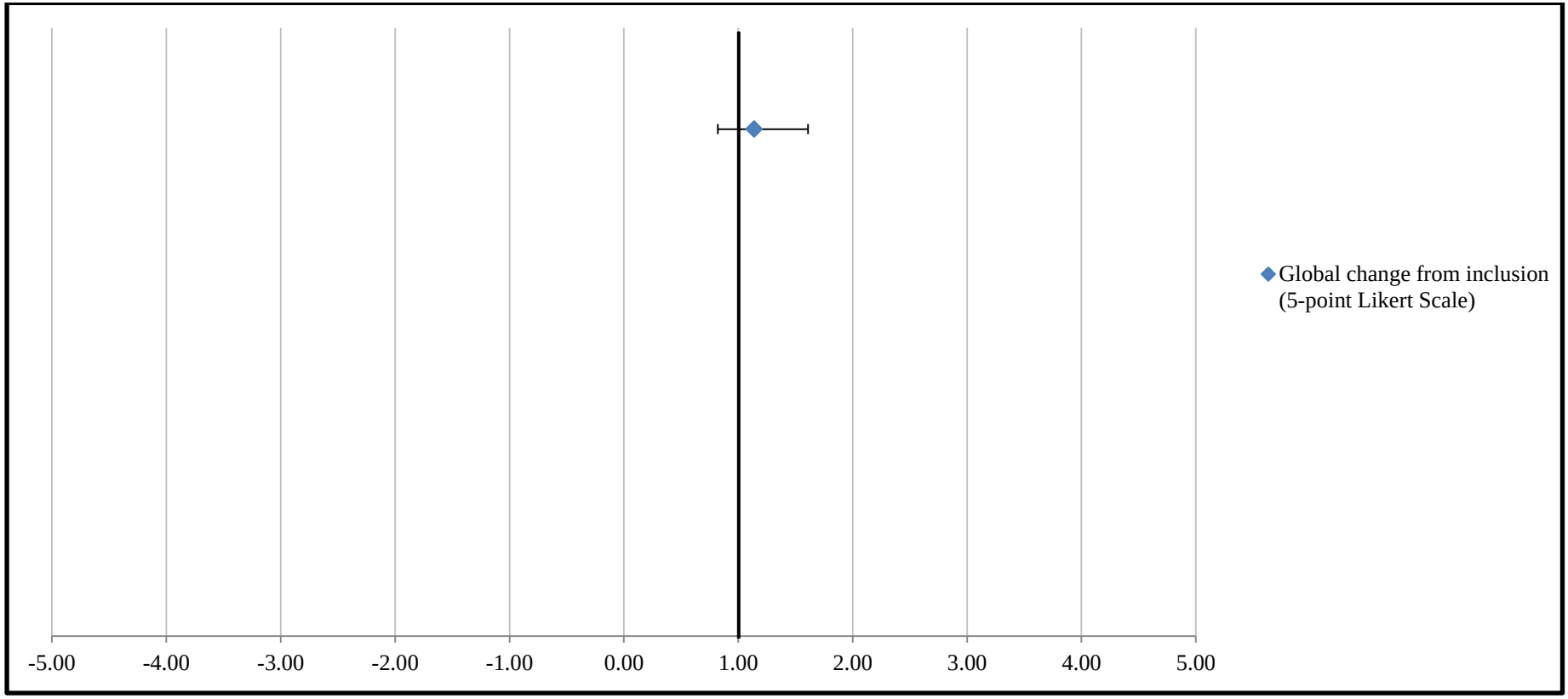

Figure 11: Relative Risk of patients reporting a successful outcome (“recovered or improved”) between the multimodal care group and subacromial decompression surgery for global change from inclusion (measured on a 5-point Likert Scale – “much worse”, “worse”, “unchanged”, “improved”, or “recovered”) (88, 89).

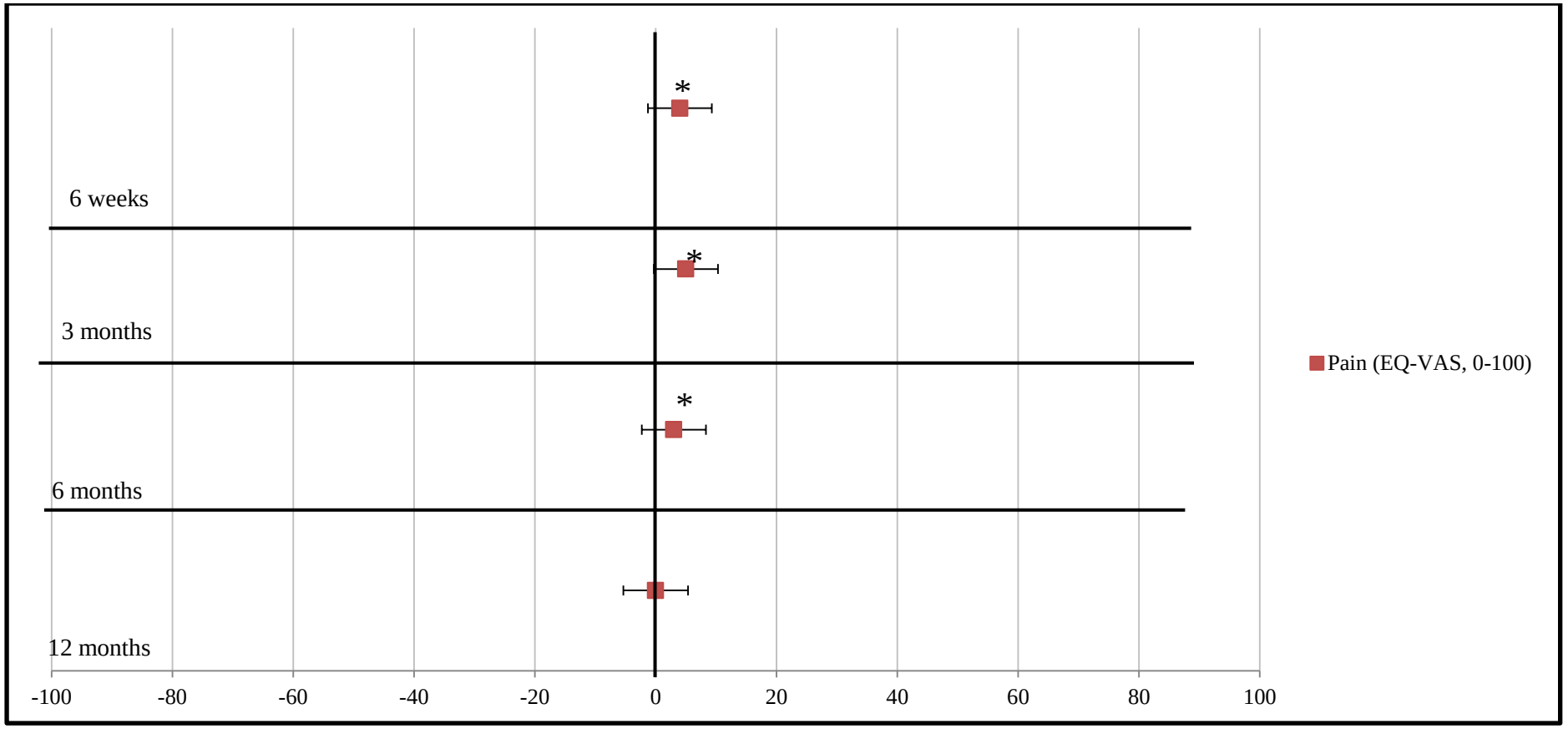

Figure 12: Difference in mean change between the multimodal care group and the corticosteroid injection group in Johansson et al., (91) measuring pain using the European Quality of Life Visual Analogue Scale (EQ-VAS). (Legend: *: Clinically important)

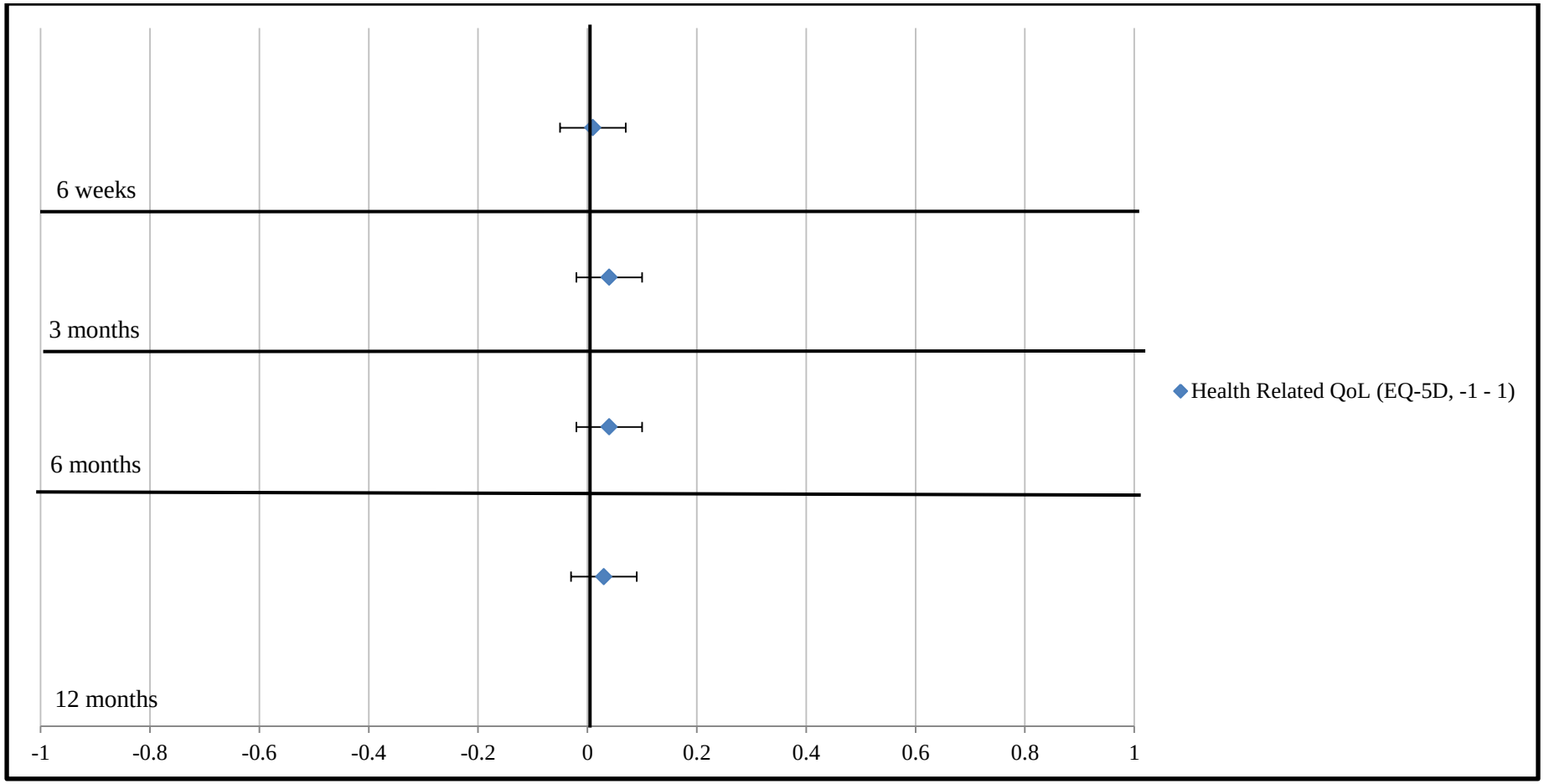

Figure 13: Difference in mean change between the multimodal care group and the corticosteroid injection group in Johansson et al., (91) measuring health related quality of life using the European Quality of life -five dimension self-report questionnaire (EQ-5D).

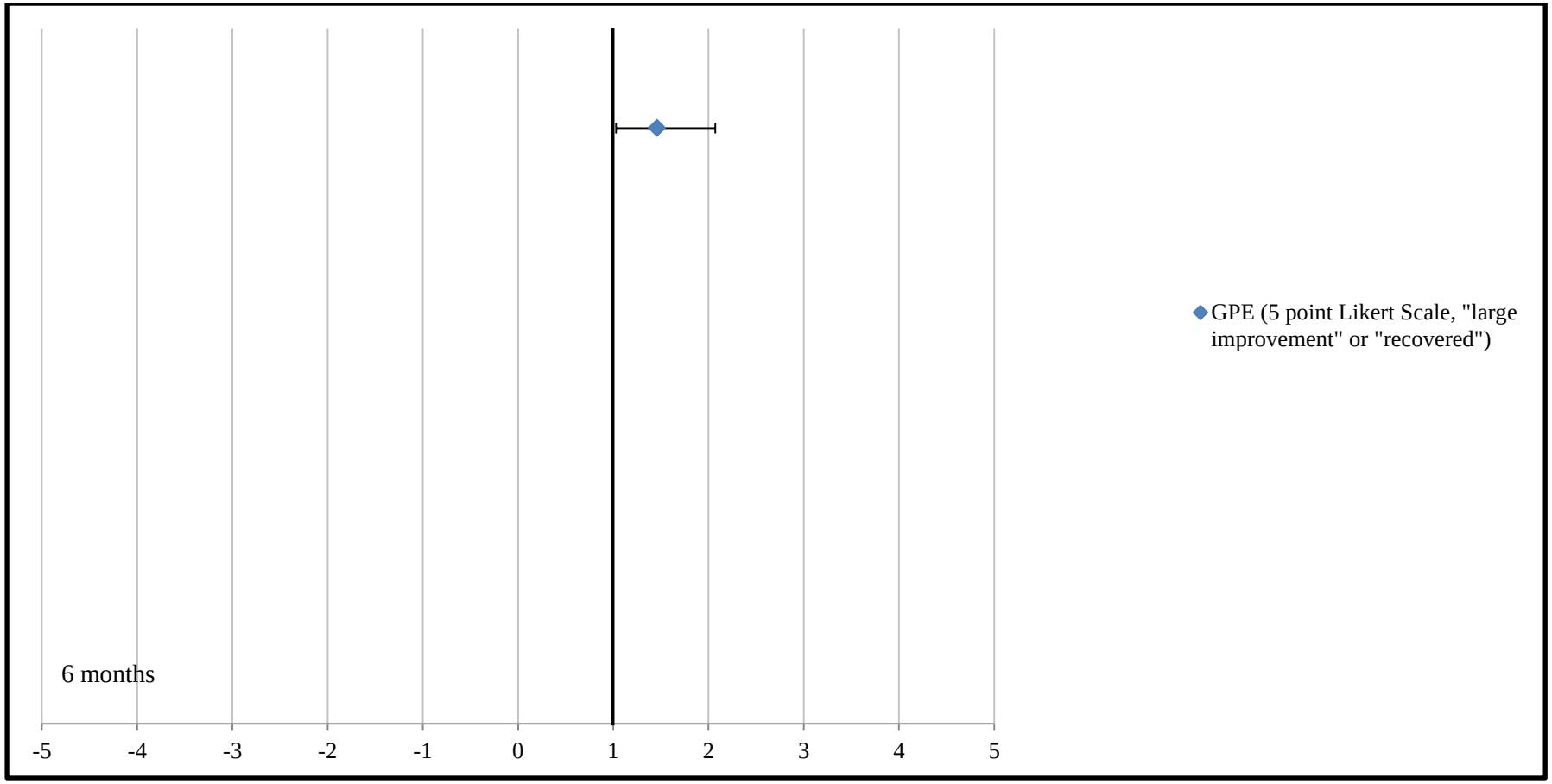

Figure 14: Relative risk of patients reporting a successful outcome (“large improvement” or “recovered”) between the multimodal care group and corticosteroid injection group for global change in symptoms (GPE) (measured on a 5-point Likert Scale – “worse”, “unchanged”, “small improvement”, “large improved”, or “recovered”) (91).

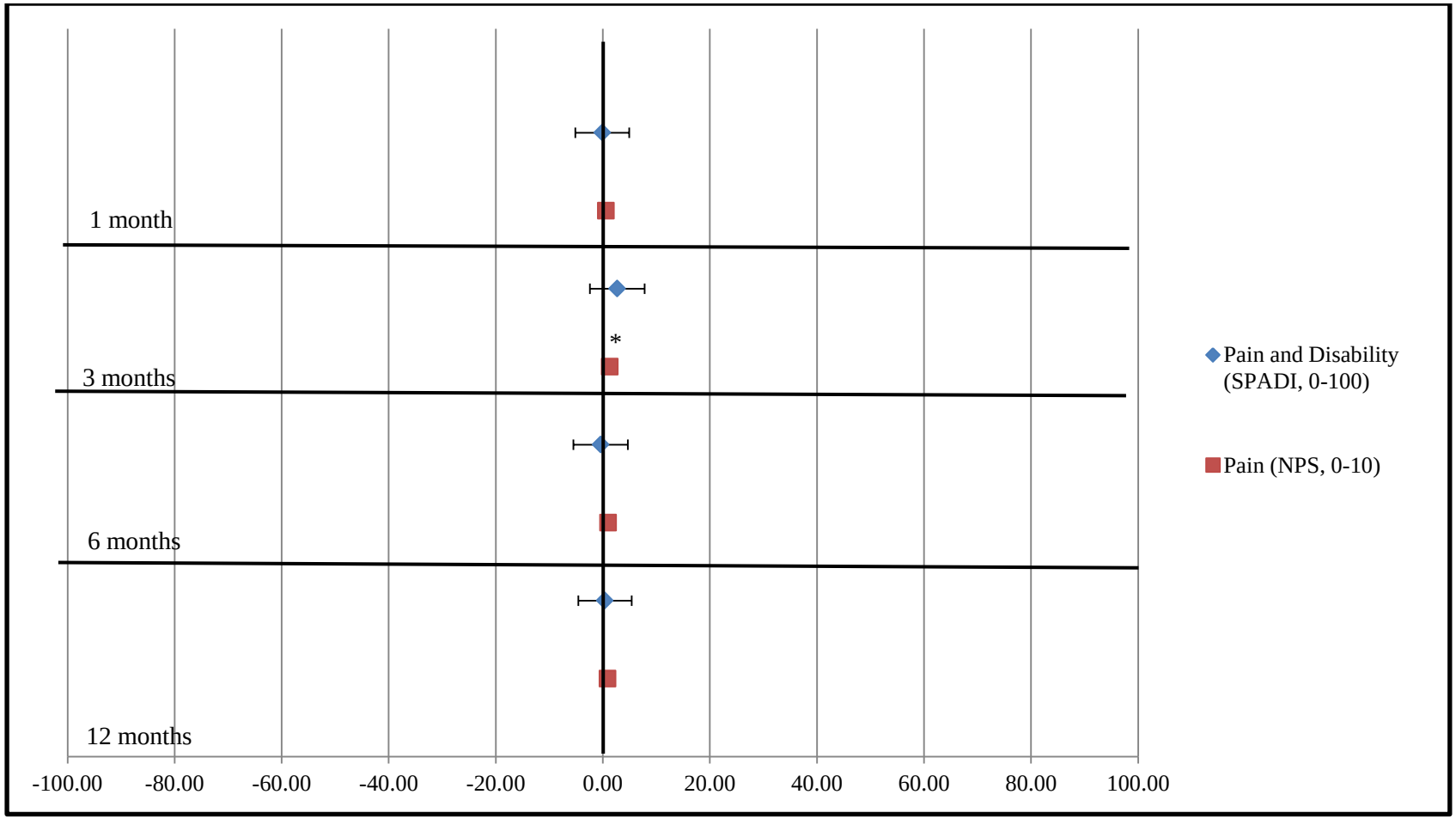

Figure 15: Difference in mean change between the multimodal care group and the corticosteroid injection group in Rhon et al., (92) measuring pain and disability using the Shoulder Pain and Disability Index (SPADI) and pain using the Numeric Rating Scale (NRS). (Legend: *: clinically important)

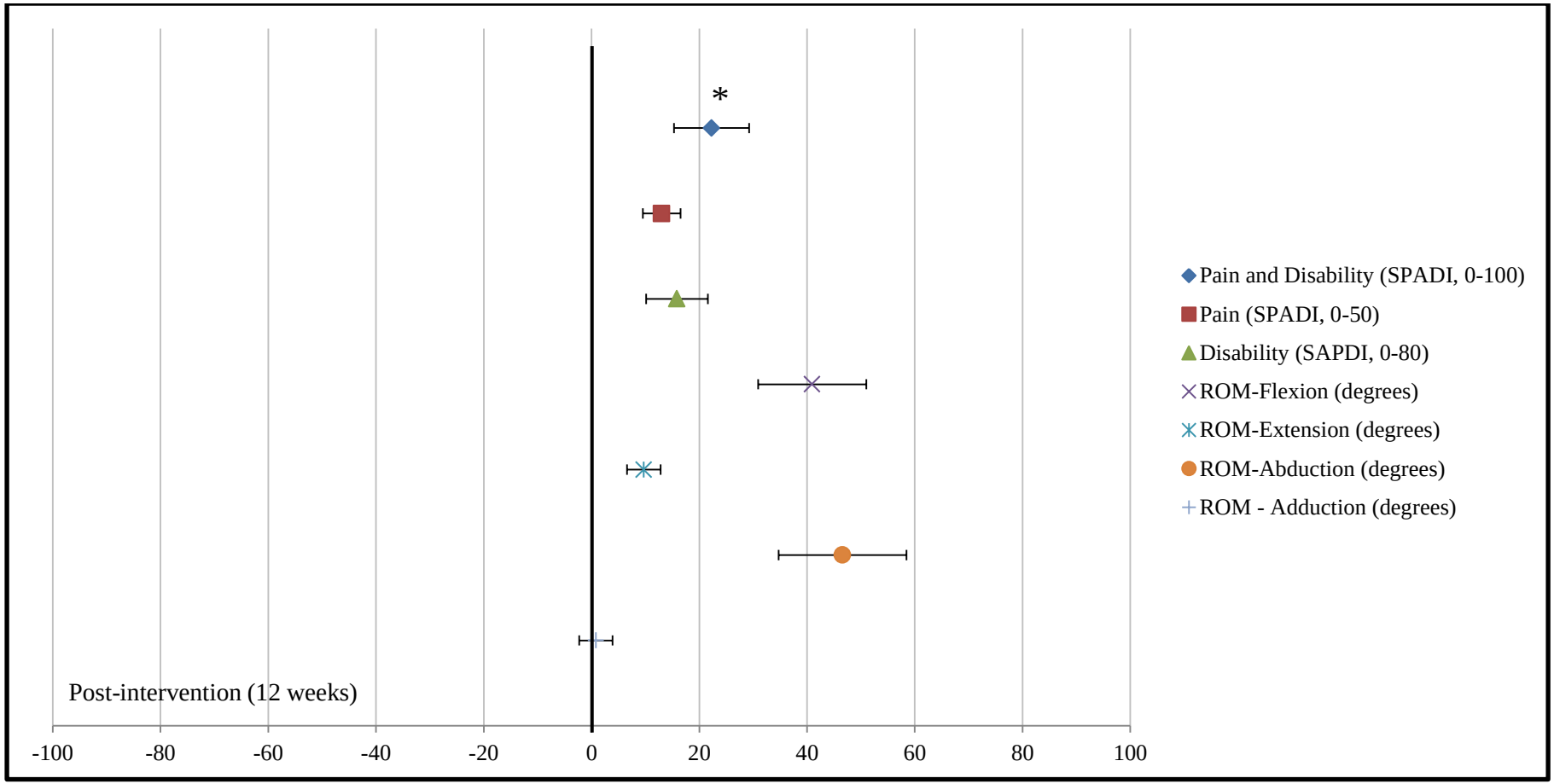

Figure 16: Difference in mean change between the diet-based multimodal care group and the exercise-based multimodal care group in Szczurko et., (93) measuring pain and disability using the Shoulder Pain and Disability Index (SPADI) and range of motion measured using a goniometer/inclinometer. (Legend: ROM: range of motion; *: clinically important)

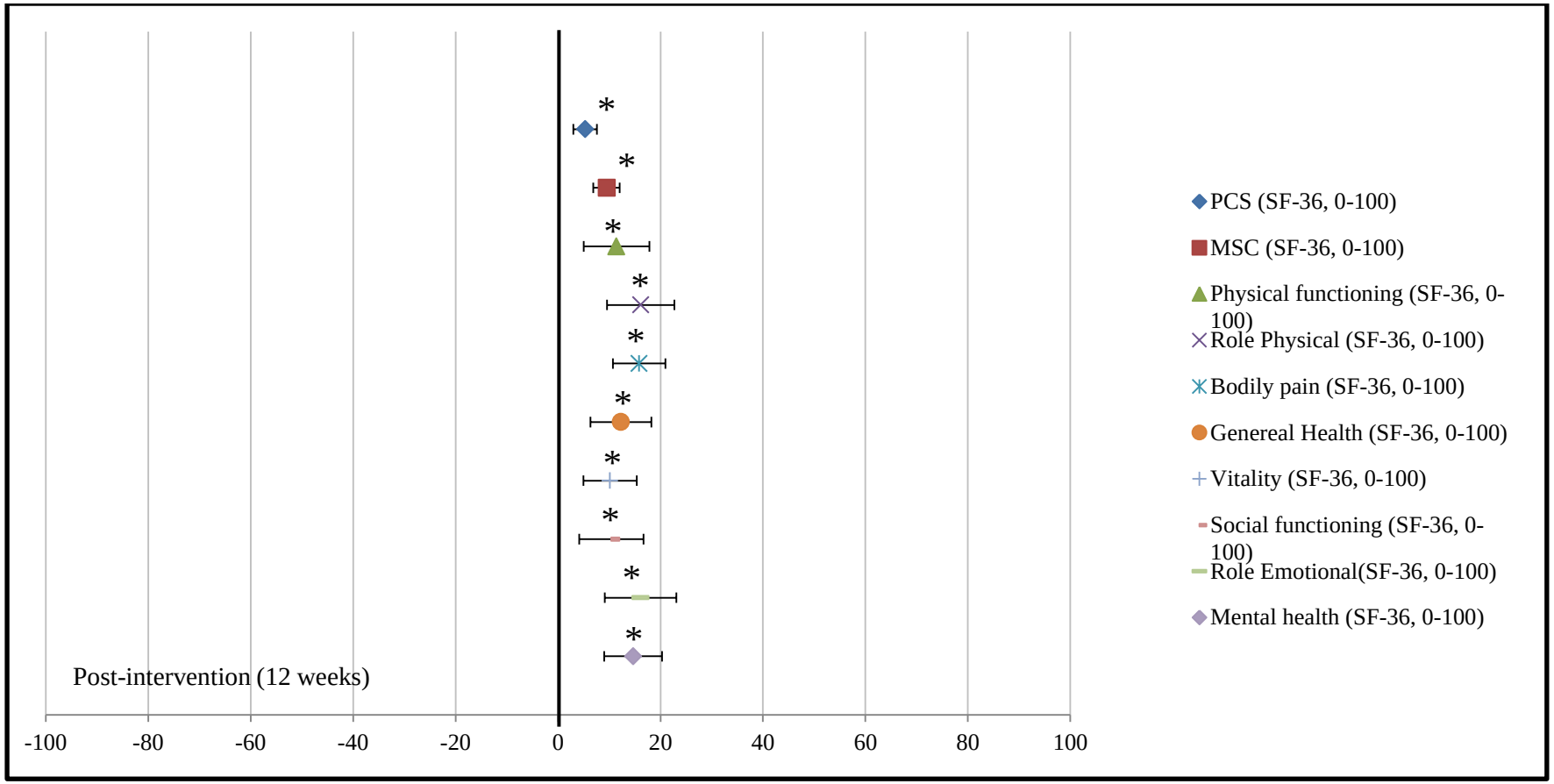

Figure 17: Difference in mean change between the diet based multimodal care group and the exercise based multimodal care group in Szczurko et., (93) measuring physical function and mental health using the Short Form- 36. (Legend: PCS: physical component scale; MCS: mental component scale; SF-36: Short-Form 36; *: Clinically important)

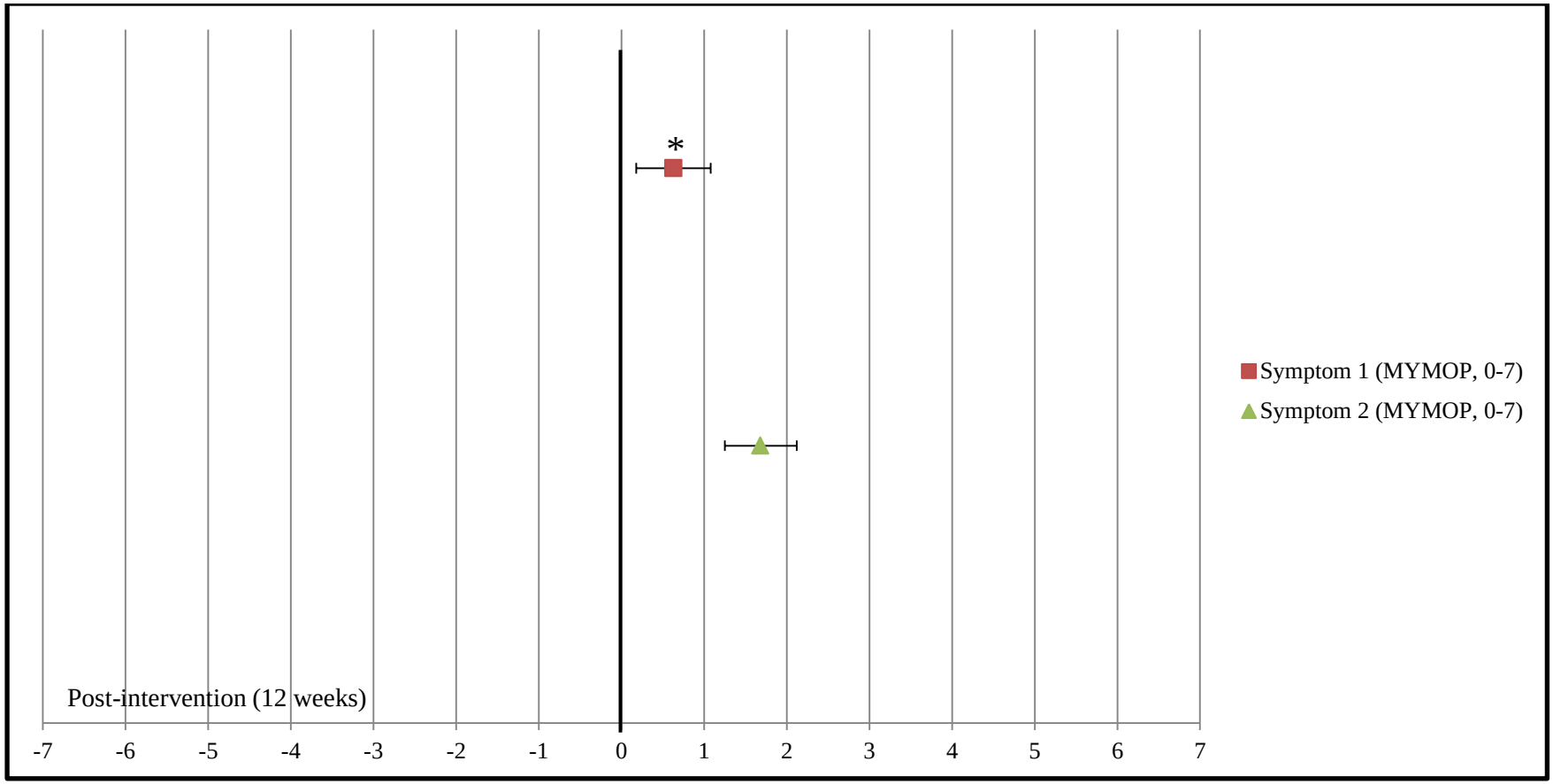

Figure 18: Difference in mean change between the diet based multimodal care group and the exercise based multimodal care group in Szczurko et., (93) measuring patient-centered outcomes using the Measure Yourself Medical Outcomes Profile (MYMOP). (Legend: *: Clinically important)

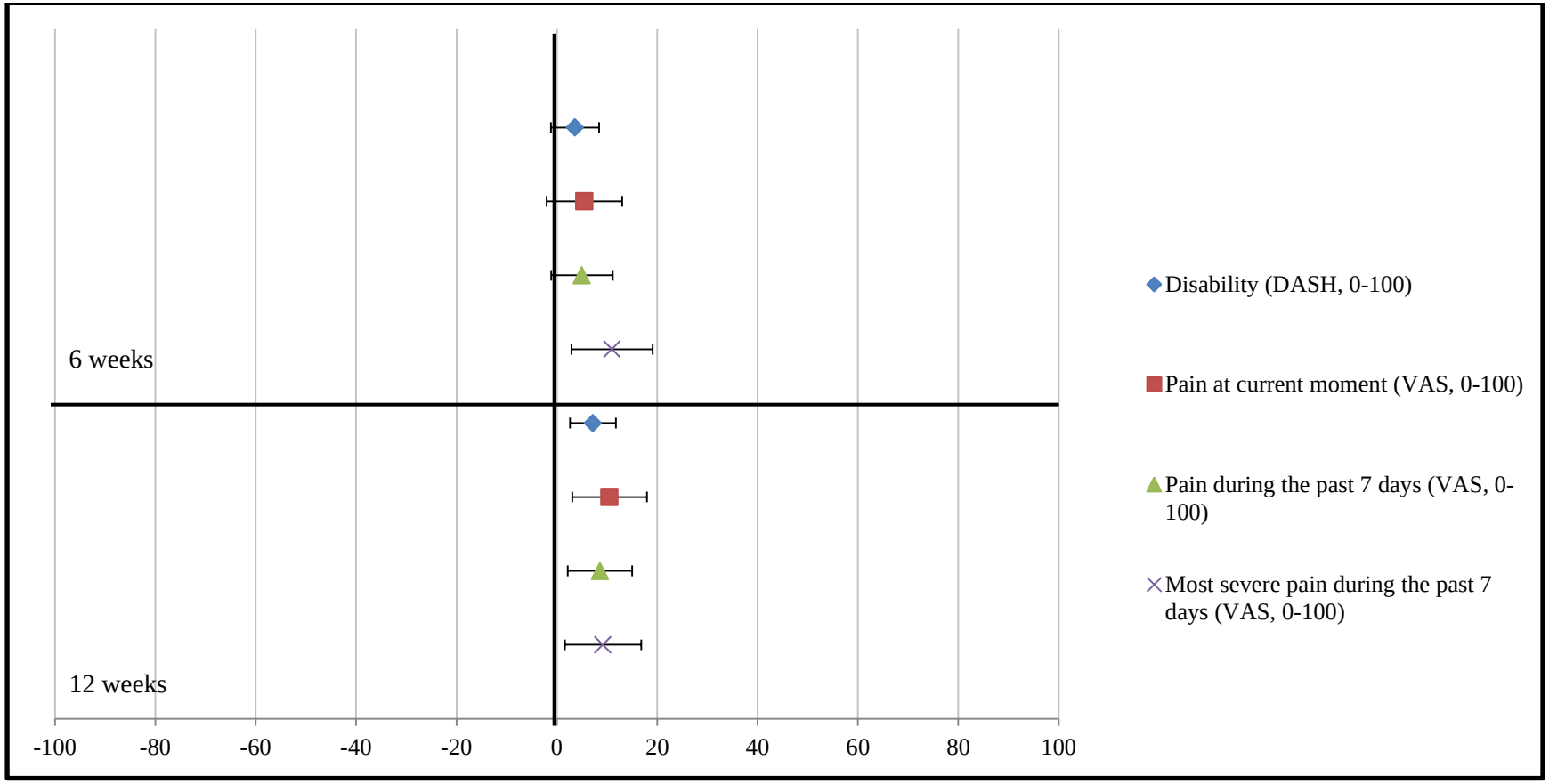

Figure 19: Difference in mean change between the multimodal care group and the 3-month wait list group in Bron et al., (83) measuring disability using the Disabilities of Arm, Shoulder and Hand (DASH) questionnaire and pain using a Visual Analogue Scale (VAS).

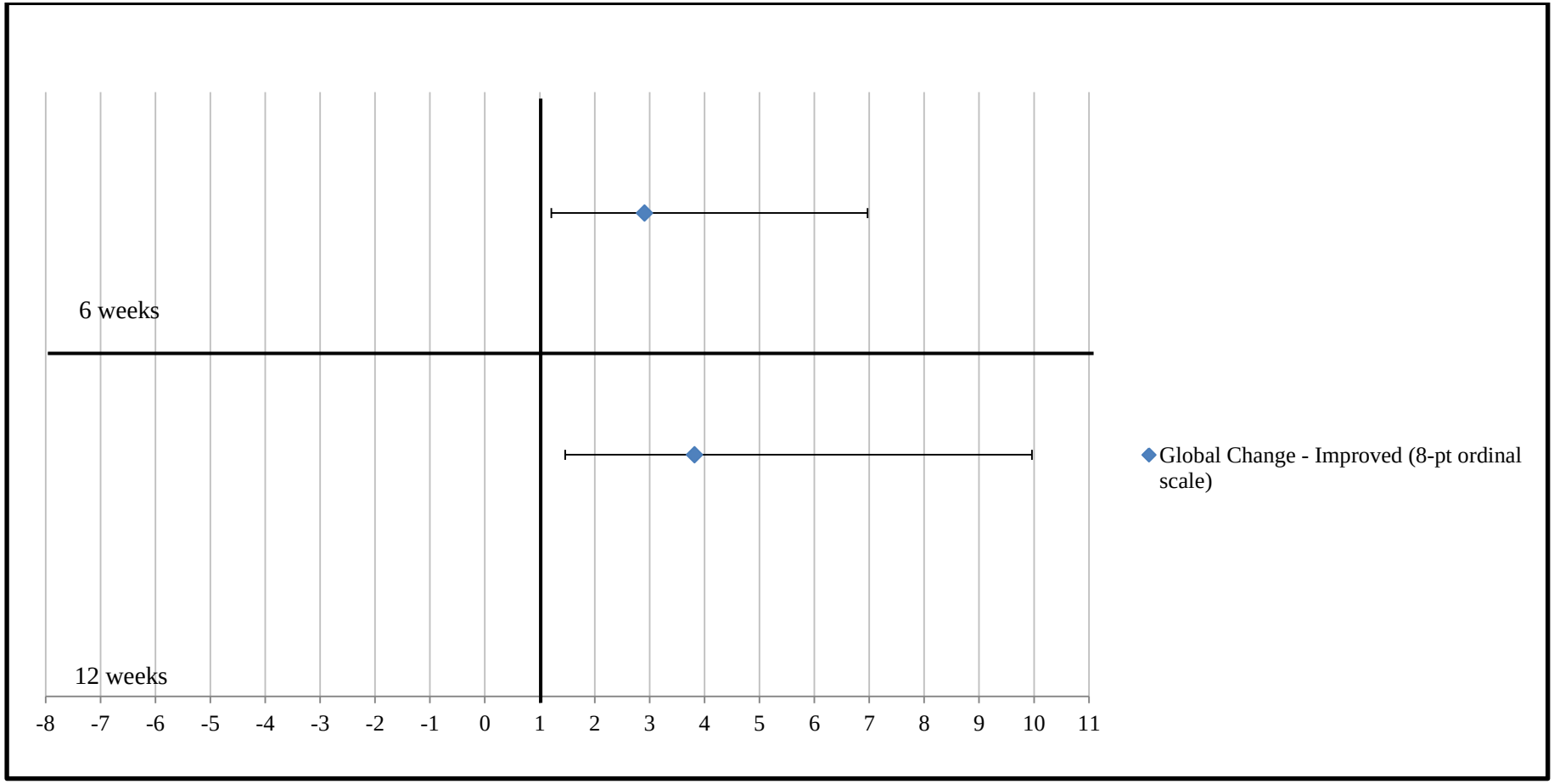

Figure 20: Relative risk of patient's global perceived change (slightly improved to completely recovered) between the multimodal care group and corticosteroid injection group measured on a 8-point Likert Scale ranging from "1: much worse" to "8: completely recovered" (83).

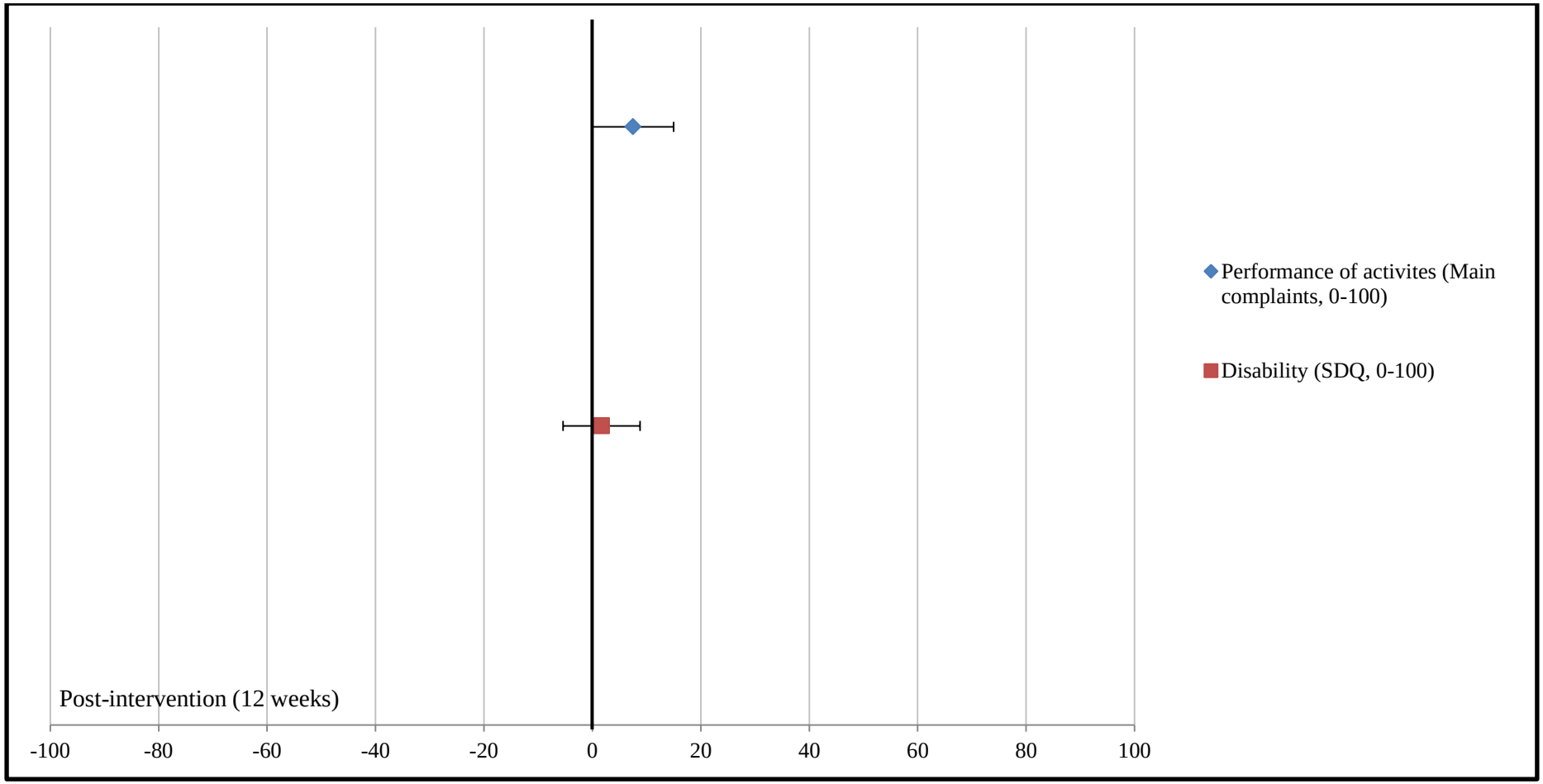

Figure 21: Difference in mean change between the exercise-based multimodal care group and usual care multimodal group in Geraets et al., (86) measuring performance of the level of daily activities using the Main Complaints Instrument and disability using the Shoulder Disability Questionnaire (SDQ).

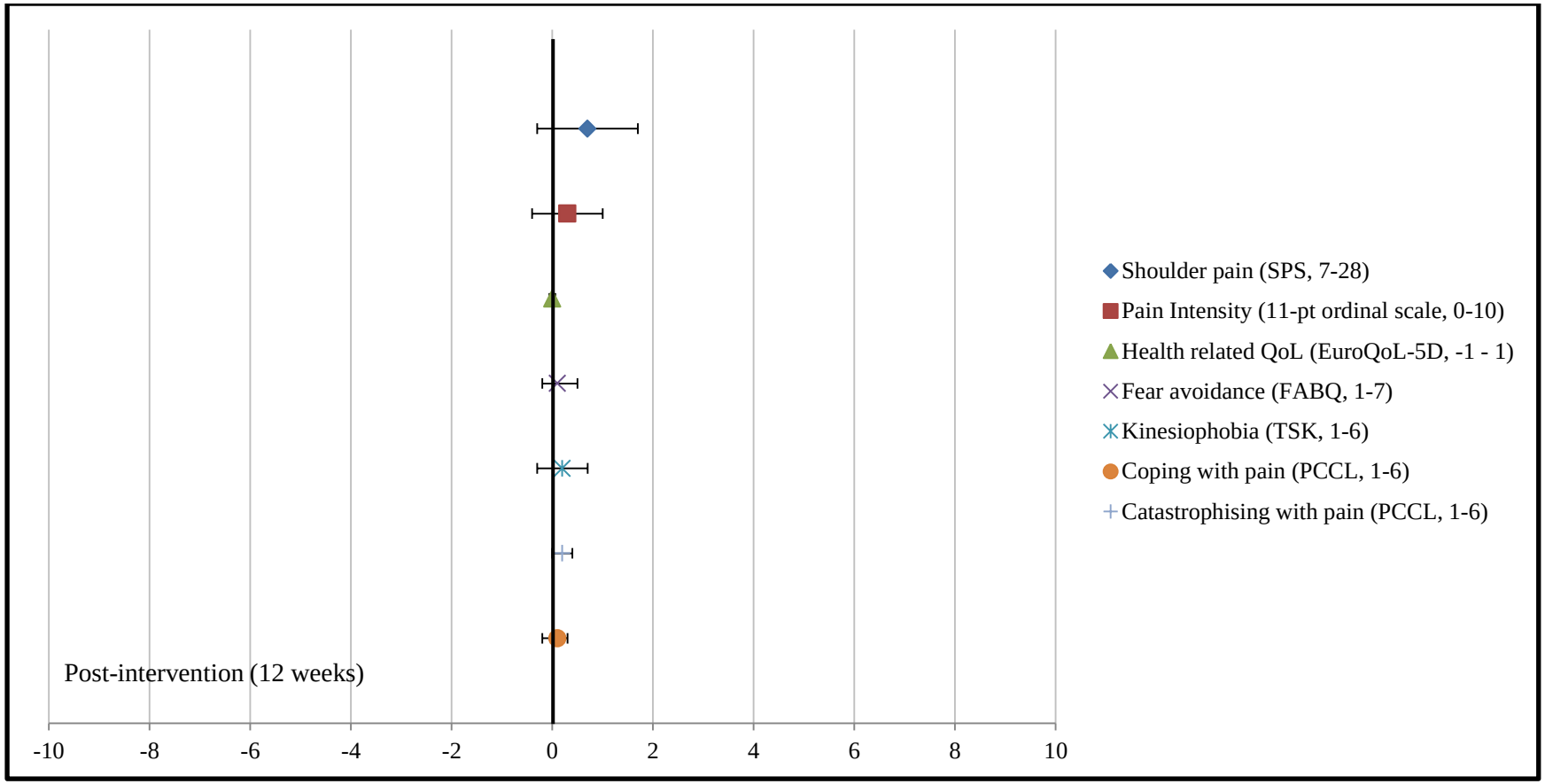

Figure 22: Difference in mean change between the exercise-based multimodal care group and usual care multimodal group in Geraets et al., (86) measuring shoulder pain, pain intensity (11-point ordinal scale,), health related quality of life (EuroQol-five dimension self-report questionnaire), fear avoidance, coping and catastrophizing with pain. (Legend: SPS: Shoulder pain Score; QoL: Quality of Life; FABQ: Fear-Avoidance Beliefs Questionnaire; TSK: Tampa Scale of Kinesiophobia; PCCL: Pain Coping and Cognition List)

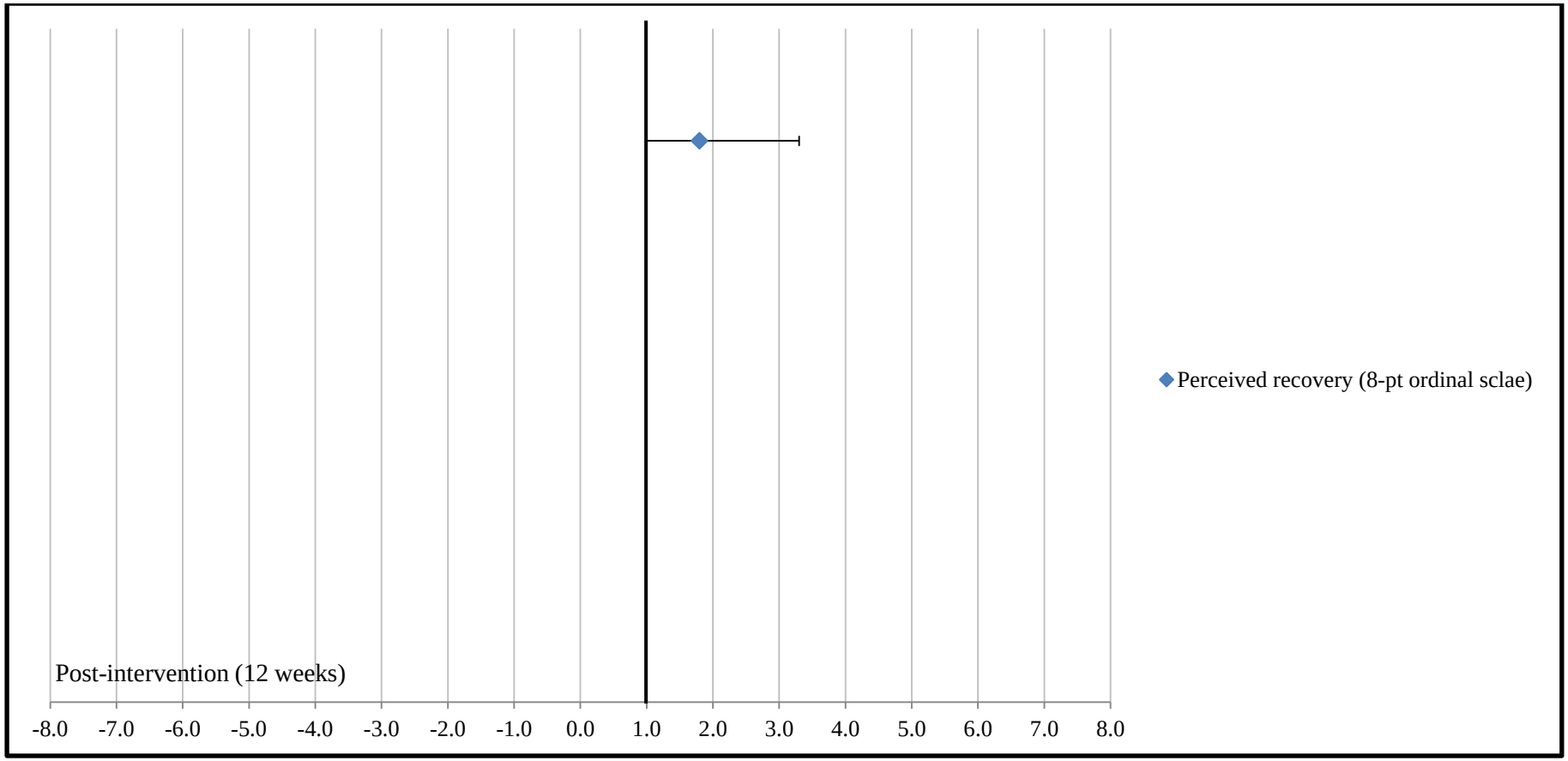

Figure 23: Relative risk of patient's global perceived recovery (slightly improved to fully recovered) between exercise-based multimodal care group and usual care multimodal group in Geraets et al., (86) measured on a 8-point Likert Scale ranging from "0: fully recovered" to "8: very much deteriorated".

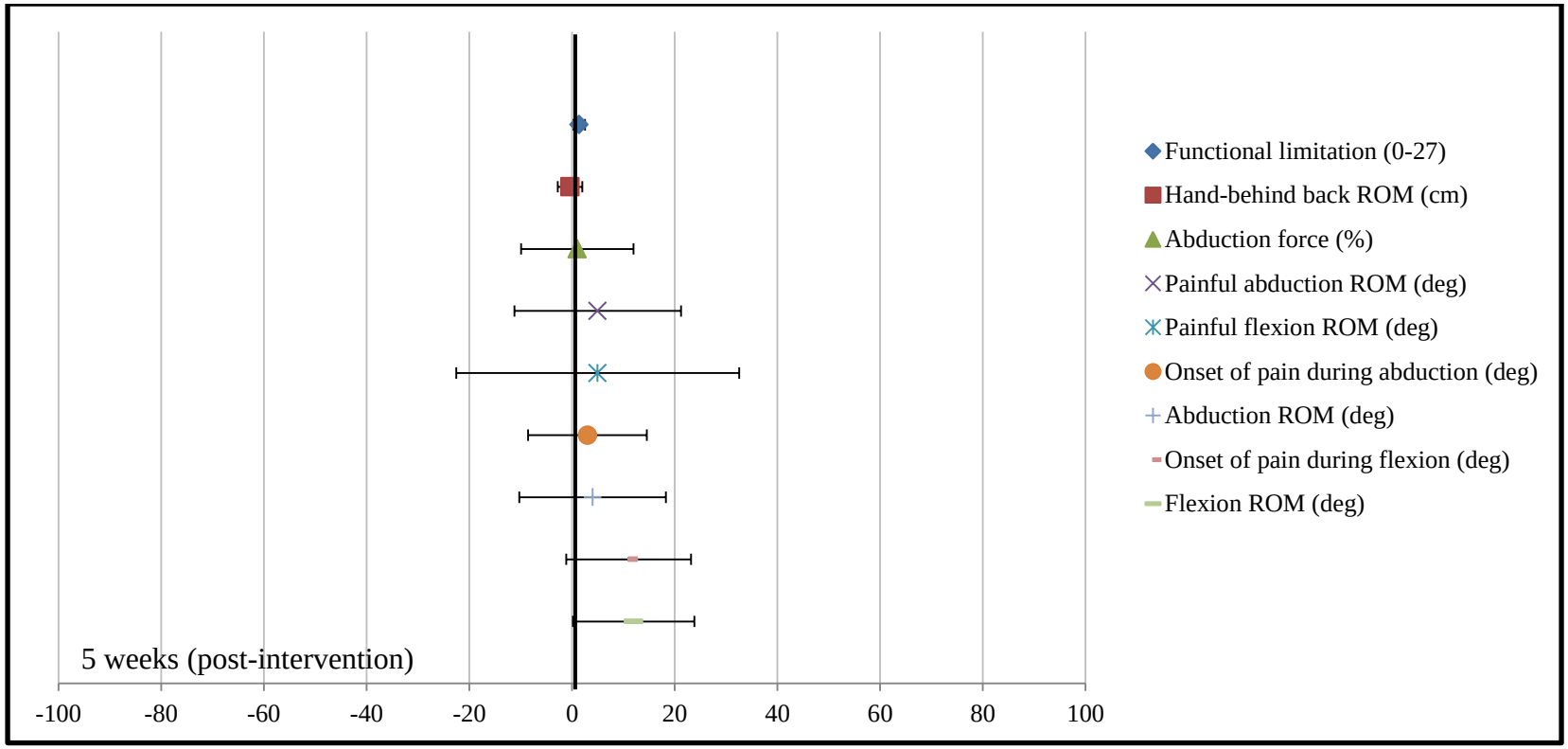

Figure 24: Difference in mean change between the multimodal care group and corticosteroid injection group in Ginn & Cohen (87) measuring functional limitation (sum of 9 questions rating the level of difficulty associated with performing 9 specified upper limb task measured on a 4-point Likert Scale "0=can perform with no shoulder pin" to "3=cannot perform because of shoulder pain"), hand-behind back range of motion, abduction force, painful abduction range of motion, painful flexion range of motion, and onset of pain during abduction. (Legend: cm: centimetre; ROM: range of motion; deg: degrees)

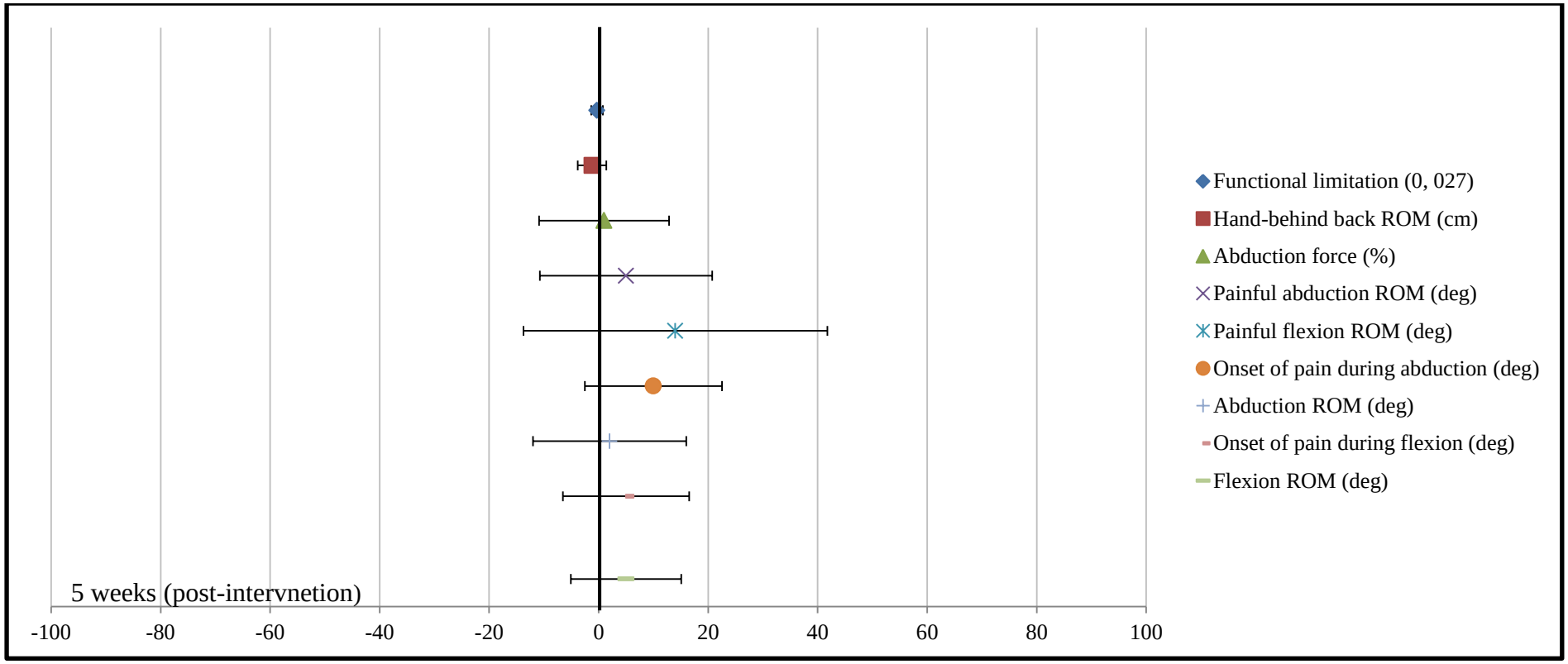

Figure 25: Difference in mean change between the multimodal care group and exercise group in Ginn & Cohen (87) measuring functional limitation (sum of 9 questions rating the level of difficulty associated with performing 9 specified upper limb task measured on a 4-point Likert Scale “0=can perform with no shoulder pin” to “3=cannot perform because of shoulder pain”), hand-behind back range of motion, abduction force, painful abduction range of motion, painful flexion range of motion, and onset of pain during abduction. (Legend: cm: centimetre; ROM: range of motion; deg: degrees)

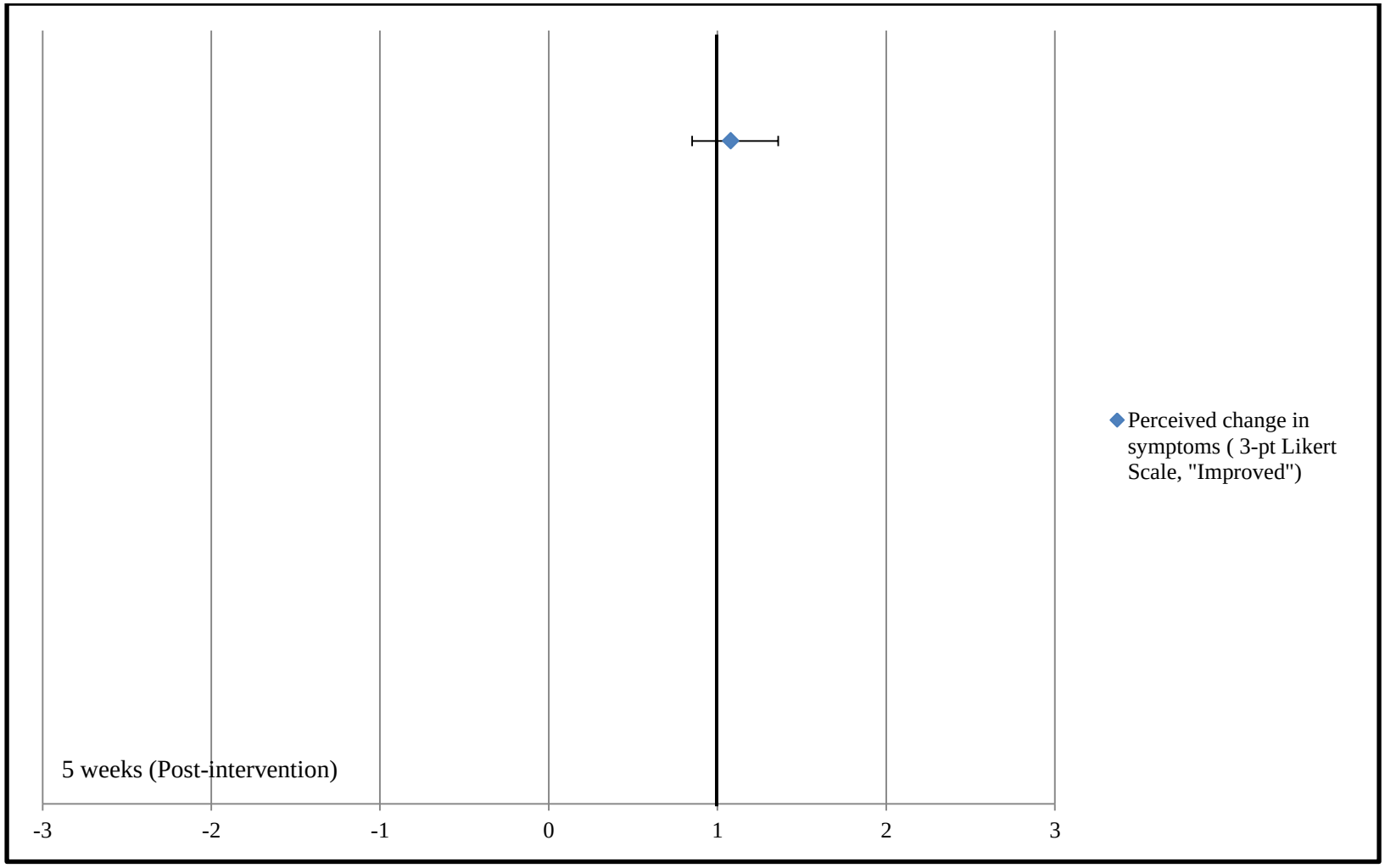

Figure 26: Relative risk of patient's global perceived change in symptoms (improved) between multimodal care group and corticosteroid injection group in Ginn & Cohen using a 3-point Likert Scale, "getting better", "staying the same" and "getting worse".

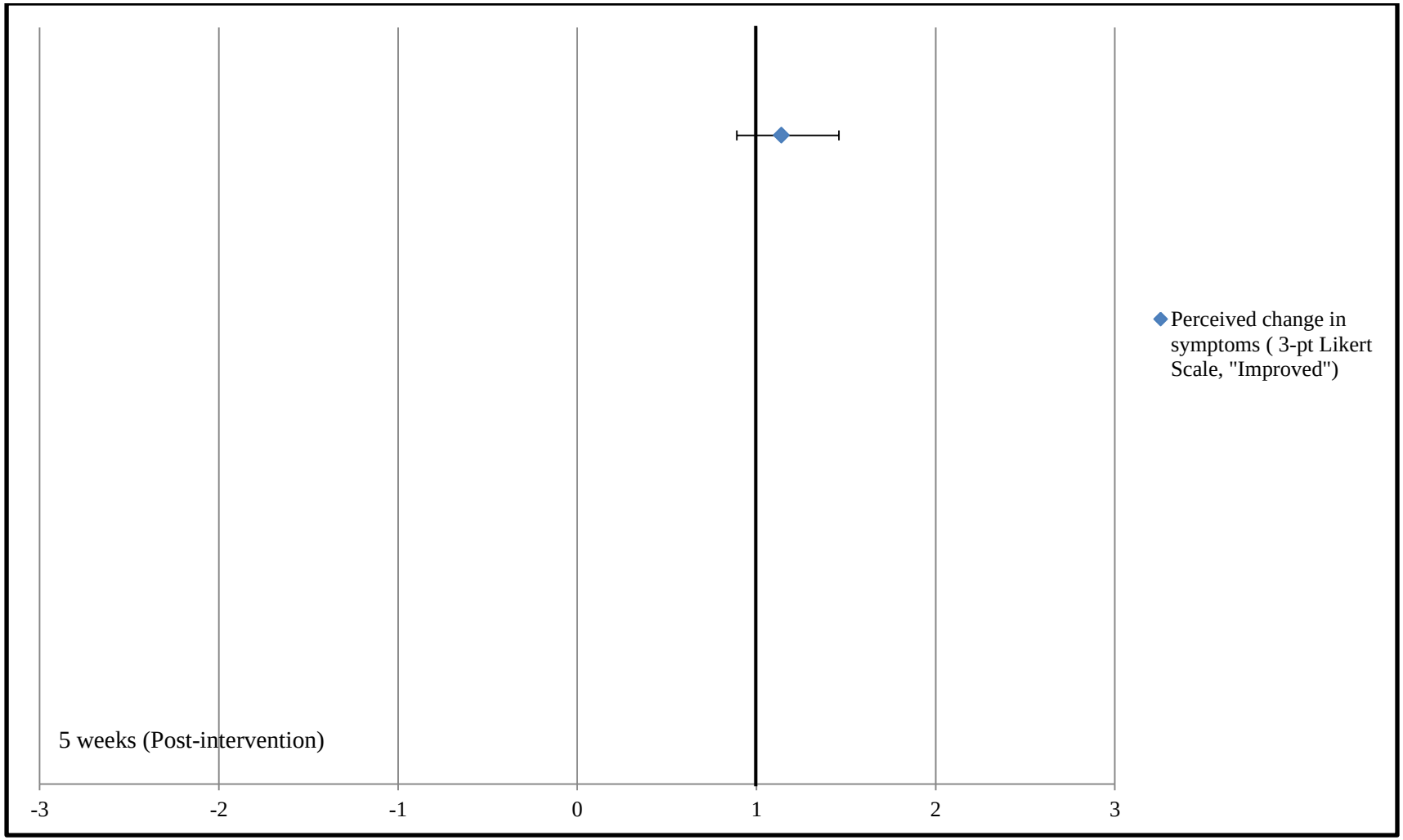

Figure 27: Relative risk of patient's global perceived change in symptoms (improved) between multimodal care group and exercise group in Ginn & Cohen (87) using a 3-point Likert Scale, "getting better", "staying the same" and "getting worse".

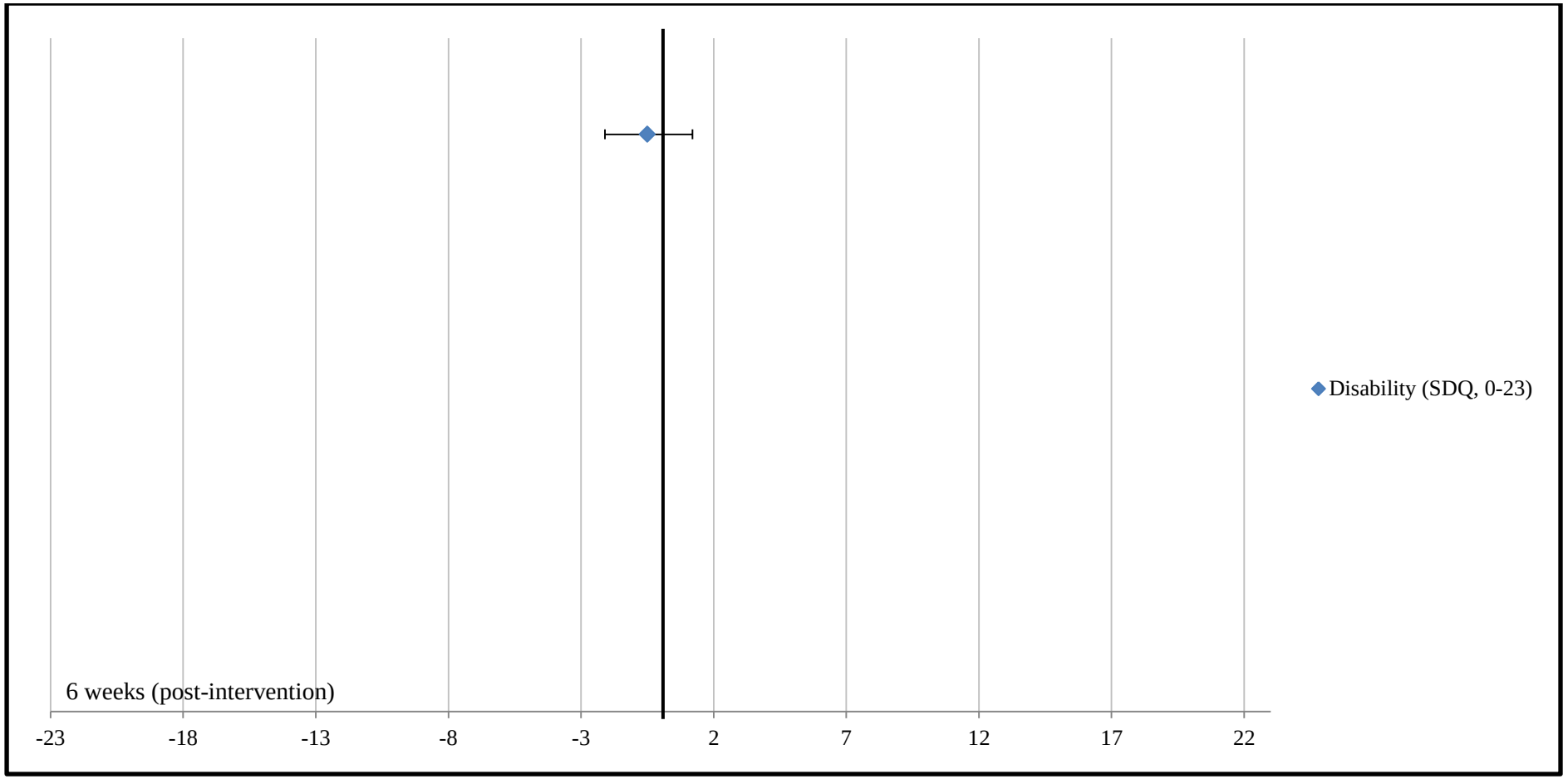

Figure 28: Difference in mean change between the multimodal care group and corticosteroid injection group in Hay et al., (90) measuring disability using the Shoulder Disability Questionnaire (SDQ).

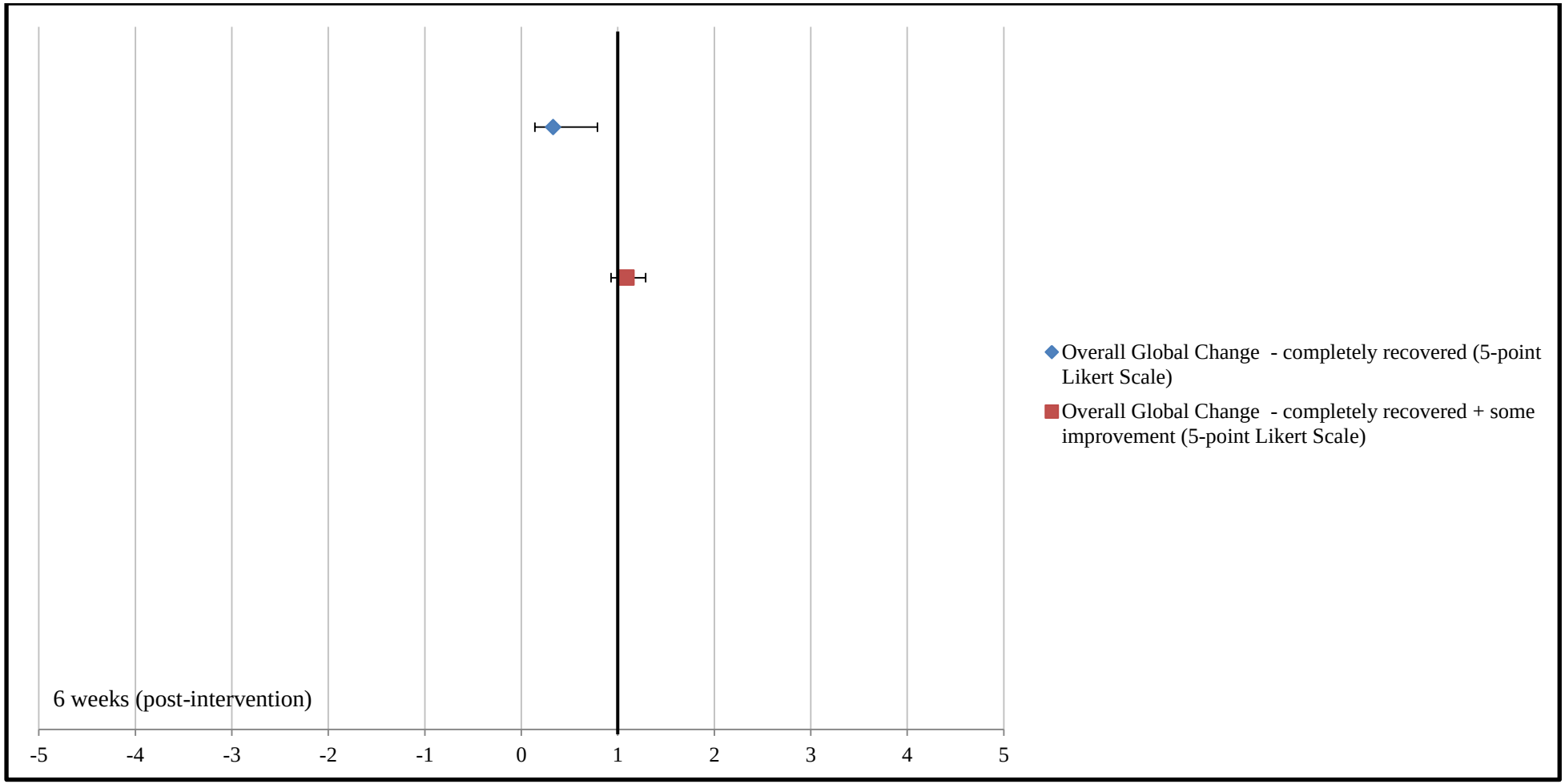

Figure 29: Relative risk of patient's overall global change in symptoms between the multimodal care group and corticosteroid injection group in Hay et al., (90) measured on a 5-point Likert Scale "complete recovered", "some improvement", "no change", "worse", and "much worse".

Appendix II: SIGN Methodology Checklist 1: Systematic Reviews and Meta-Analyses

S I G N	**Methodology Checklist 1: Systematic Reviews and Meta-analyses** SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C,. et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10. Available from http://www.biomedcentral.com/1471-2288/7/10 [cited 10 Sep 2012]*

Study identification (*Include author, title, year of publication, journal title, pages*)	
Guideline topic:	Key Question No:
Before completing this checklist, consider: 1. Is the paper a systematic review or meta-analysis? IF NO reject. IF YES continue. 2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.	
Checklist completed by:	

Section 1: Internal validity		
In a well conducted systematic review:		***Does this study do it?***
1.1	The study addresses a clearly defined research question.	Yes ☐ No ☐ Can't say ☐
1.2	At least two people should select studies and	Yes ☐ No ☐

	extract data.	Can't say ☐
1.3	A comprehensive literature search is carried out.	Yes ☐ No ☐ Can't say ☐ Does not apply ☐
1.4	The authors clearly state if or how they limited their review by publication type.	Yes ☐ No ☐
1.5	The included and excluded studies are listed.	Yes ☐ No ☐
1.6	The characteristics of the included studies are provided.	Yes ☐ No ☐
1.7	The scientific quality of the included studies is assessed and documented.	Yes ☐ No ☐

1.8	The scientific quality of the included studies was assessed appropriately.	Yes ☐ No ☐ Can't say ☐
1.9	Appropriate methods are used to combine the individual study findings.	Yes ☐ No ☐ Can't say ☐
1.10	The likelihood of publication bias is assessed.	Yes ☐ No ☐ Can't say ☐
1.11	Conflicts of interest are declared.	Yes ☐ No ☐
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review?	High quality (++) ☐ Acceptable (+) ☐ Low quality (-) ☐ Irrelevant/ wrong type – reject (0) ☐
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes ☐ No ☐
2.3	**Notes:**	

Appendix III: MEDLINE through OVID Search Strategy

1. Shoulder Pain/

2. Shoulder Impingement Syndrome/

3. Shoulder Joint/in [Injuries]

4. Rotator Cuff/

5. Shoulder/in [Injuries]

6. "Sprains and Strains"/

7. "shoulder*".ab,ti.

8. 6 and 7

9. (shoulder* and (pain* or sprain* or strain* or injur* or impair* or impingement)).ab,ti.

10. (shoulder* and (tendinopathy or tendinitis or tendonitis or capsulitis)).ab,ti.

11. ((glenohumeral or scapul* or acromioclavicular) and (pain* or sprain* or strain* or injur*)).ab,ti.

12. (rotator cuff and (sprain* or strain* or tear* or bursitis tendinitis or impingement)).ab,ti.

13. ((supraspinatus or infraspinatus or subscapularis or teres minor or teres major or trapezius or deltoid or bicep* or bicipital or coracobrachialis) and (impingement or strain* or tear* or pain*)).ab,ti.

14. biceps tend?nitis.ab,ti.

15. painful arc.ab,ti.

16. (shoulder and capsul* and (sprain* or tear*)).ab,ti.

17. or/1-5

18. or/8-16

19. or/17-18

20. Combined Modality Therapy/

21. (pragmatic and (randomized clinical trial or RCT or approach*)).ab,ti.

22. "physical modalit*".ab,ti.

23. (team* and (care or health or healthcare or medical)).ab,ti.

24. (grouped and (care or approach)).ab,ti.

25. (care and (package or packages)).ab,ti.

26. (collaborat* and (treatment* or therap* or care or procedure* or approach or rehabilitat*)).ab,ti.

27. (combined and (treatment* or therap* or care or procedure* or approach or rehabilitat*)).ab,ti.

28. (comprehensive and (treatment* or therap* or care or procedure* or approach or rehabilitat*)).ab,ti.

29. (integrated and (treatment* or therap* or care or procedure* or approach or rehabilitat*)).ab,ti.

30. (disciplin* and (approach or care)).ab,ti.

31. (pragmatic and (approach or care)).ab,ti.

32. ((multicentre* or multi-centre* or multicenter* or multi-center*) and (treatment* or therap* or care or procedure* or approach* or rehabilitat*)).ab,ti.

33. Multicenter Study.pt.

34. (treatment* or therap* or care or procedure* or approach or rehabilitat*).ab,ti.

35. (co-ordinat* or coordinat*).ab,ti.

36. (multimodal* or multi-modal* or multi modal*).ab,ti.

37. (interdisciplin* or inter-disciplin* or inter disciplin*).ab,ti.

38. (interprofessional or inter-professional).ab,ti.

39. (multidisciplin* or multi-disciplin* or multi disciplin*).ab,ti.

40. or/20-39

41. Randomized Controlled Trials as Topic/

42. Controlled Clinical Trials as Topic/

43. Clinical Trials as Topic/

44. exp case-control studies/

45. exp Cohort Studies/

46. Double-Blind Method/

47. Single-Blind Method/

48. Placebos/

49. randomized controlled trial.pt.

50. controlled clinical trial.pt.

51. comparative study.pt.

52. (meta analys* or meta-analys* or metaanalys*).ab,ti.

53. (cohort and (study or studies or analys*)).ab,ti.

54. (random* and (control* or clinical or allocat*)).ab,ti.

55. (case adj control*).ab,ti.

56. ((double or single) and blind*).ab,ti.

57. "placebo*".ab,ti.

58. (comparative and (study or studies)).ab,ti.

59. or/41-58

60. 19 and 40 and 59

61. limit 60 to (english language and humans and yr="1990 -Current")

Appendix IV: SIGN Methodology Checklist 2: Controlled Trials

SIGN	**Methodology Checklist 2: Controlled Trials**

Study identification (*Include author, title, year of publication, journal title, pages*)

Guideline topic:	Key Question No:	Reviewer:

Before completing this checklist, consider:

1. Is the paper a **randomised controlled trial** or a **controlled clinical trial**? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist. If it is a **controlled clinical trial** questions 1.2, 1.3, and 1.4 are not relevant, and the study cannot be rated higher than 1+
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist.

Reason for rejection: 1. Paper not relevant to key question ☐ 2. Other reason ☐ (please specify):

Section 1: Internal validity

In a well conducted RCT study…		*Does this study do it?*
1.1	The study addresses an appropriate and clearly focused question.	Yes ☐ No ☐ Can't say ☐
1.2	The assignment of subjects to treatment groups is randomised.	Yes ☐ No ☐ Can't say ☐
1.3	An adequate concealment method is used.	Yes ☐ No ☐ Can't say ☐
1.4	Subjects and investigators are kept 'blind' about treatment allocation.	Yes ☐ No ☐ Can't say ☐
1.5	The treatment and control groups are similar at the start of the trial.	Yes ☐ No ☐ Can't say ☐
1.6	The only difference between groups is the treatment under investigation.	Yes ☐ No ☐ Can't say ☐

1.7	All relevant outcomes are measured in a standard, valid and reliable way.	Yes ☐ No ☐ Can't say ☐
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).	Yes ☐ No ☐ Can't say ☐ Does not apply ☐
1.10	Where the study is carried out at more than one site, results are comparable for all sites.	Yes ☐ No ☐ Can't say ☐ Does not apply ☐

SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	**How well was the study done to minimise bias?** ***Code as follows:***	High quality (++)☐ Acceptable (+)☐ Unacceptable – reject 0 ☐
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	
2.4	**Notes.** Summarise the authors' conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.	

Appendix V: Tables

Table 1: Risk of Bias for Systematic Reviews based on Scottish Intercollegiate Guidelines Network Criteria (48)

Author(s), Year	Research question	Study selection and data extraction	Literature Search	Limiting review by publication type	List of included and excluded studies	Characteristics of included studies	Scientific quality documented	Scientific quality assessed appropriately	Appropriate methods for combining findings	Publication bias assessed	Conflicts of interest declared
Green et al., 2003 (19)	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y
Trampas and Kitsios, 2006 (20)	Y	Y	Y	Y	Y	Y	Y	Y	Y	CS	N
McHardy et al., 2008 (49)	Y	CS	Y	Y	N	N	Y	N	N	CS	N
Pribicevic et al., 2010 (11)	Y	CS	Y	N	N	Y	N	N	N	CS	N
Nyberg etl al., 2010 (50)	Y	N	Y	Y	Y	Y	Y	N	Y	N	N
Brantingham et al., 2011 (51)	Y	Y	Y	Y	N	N	Y	Y	N	CS	Y

Acronyms: Y: Yes; N: No; CS: Can't Say (insufficient detail to allow an assessment to be made); NA: Not Applicable

Table 2: Evidence table for Accepted Randomized Controlled Trials on the Effectiveness of Multimodal for the Management of Soft Tissue Injuries of the Shoulder

Author(s), Year	Subjects and Setting; Number (n) Enrolled	Interventions; Number (n) of Subjects	Comparisons; Number (n) of Subjects	Follow-up	Outcomes	Key Findings
Bennell et al., 2010 (82)	Adults (≥18 y.o.) recruited through GP and print/radio media between 2004 and 2007 in Australia. Case Definition: shoulder pain (>3 months; >3/10 severity on NRS during movement), and positive impingement test with diagnosis of chronic rotator cuff disease. (n=120)	Multimodal care by a PT: 1) massage, mobilisation of glenohumeral joint, scapular retraining, postural taping, spinal mobilisation (10 30-45 minutes visits/10 weeks); 2) daily home exercise (twice daily for first week; daily to 22 weeks); 3) behavioural strategies (education, goal setting, motivation, positive reinforcement) (n=59)	Placebo by a PT: Sham ultrasound therapy plus non-therapeutic gel to the shoulder region (10 10-minutes visits/10 weeks). (n=61)	11 and 22 weeks	Primary Outcomes: Shoulder pain and disability (SPADI, 0-100), pain (NRS, 0-10), perceived global improvement (5 point Likert Scale ranging from "1=much worst" to "5=much better") Secondary outcomes: Health related QoL (SF-36, 0-100), the assessment of QoL (AQoL), isometric shoulder strength for abduction & internal/external rotation (Nicholas Manual Muscle tester using dynamometer), pain at rest, weakness on movement, stiffness on movement and interference with activity (NRS, 0-10).	Difference in mean change (Multimodal Care – Placebo): SPADI (0-100) 11 weeks: Total: 3.6 (95% CI -2.1; 9.4); Pain: 3.2 (95% CI -3.2; 9.6); Function: 4.7 (95% CI -0.1; 9.5); 22 weeks: Total: 7.1 (95% CI 0.3; 13.9); Pain: 6.8 (95% CI -0.7; 14.3); Function: 7.6 (95% CI 1.8; 13.4); Pain on movement (NRS 0-10) 11 weeks: 0.7 (95% CI -0.1; 1.5); 22 weeks: 0.9 (95% CI -0.03; 1.7); Global Change (much better) 11 weeks: Overall: RR 1.43 (95% CI: 0.87; 2.34); Pain: RR 1.18 (95% Cl: 0.72; 1.91); Strength: RR 2.90 (95% CI: 1.32; 6.39); Stiffness: RR 1.65 (95% CI: 0.91; 2.99) 22 weeks: Overall: RR 1.39 (95% CI: 0.94; 2.03); Pain: RR 1.33 (95% CI: 0.92; 1.94); Strength RR 1.69 (95% CI: 0.97; 2.95): Stiffness: RR 1.49 (95% CI: 0.92; 2.41) Post-intervention, patient's global change (strength) favoured multimodal care. SPADI (Total & Function) at 22 weeks was statistically significant; however this change is not clinically significant. Secondary outcomes: Difference in mean change (multimodal care – Placebo): SF-36 (0-100)

						11 weeks: PCS: 5.7 (95% CI -2.1; 13.6); 22 weeks: PCS: 6.3 (95% CI -2.0; 14.5); No statistically significant or clinically important difference between groups for all the other outcomes.
Bron et al., 2011 (83)	Adults (18-65 y.o.) self or GP referral for PT, between 2007 and 2009 in the Netherlands Case Definition: unilateral non-traumatic shoulder pain (≥ 6 months). (n=72)	Multimodal care by a PT (12 visit /12 weeks): Soft tissue – compression; deep stroking or strumming; intermittent cold; stretching exercise; daily home relaxation exercises; heat (≥2 times/day); ergonomic advice and postural instructions. (n=37)	Wait List: Received PT after 12 weeks. (n=35)	12 weeks	<u>Primary Outcome</u>: Physical function and symptoms (DASH, 0-100) <u>Secondary Outcomes</u>: Pain at current moment (VAS-P1, 0-100); pain during the past 7 days (VAS-P2, 0-100); most severe pain during the past 7 days (VAS-P3, 0-100); Global Perceived Effect (8-pt ordinal scale ranging from "1 = much worse" to "8 = completely recovered"); Passive ROM (handheld digital inclinometer); MTrP palpation of the shoulder muscles.	<u>Difference in mean change (Multimodal Care– Wait List):</u> 3 months: <u>DASH (0-100)</u> 7.20 (95% CI 2.61; 11.79)* <u>GPE improved:</u> RR 3.82 (95% CI 1.46; 9.96)* No statistically significant or clinically important differences for all other outcomes.
Engebretsen et al. (2009) & Engebretsen et al. (2011) (84, 85)	Adults (18-70 y.o.), outpatient clinic from Norway between 2006 and 2008. Case Definition: subacromial shoulder pain (≥3 months). (n=104)	Multimodal care by a PT (2 visits per week /maximum 12 weeks): posture and endurance exercise of rotator cuff and subacromial structures; manual techniques; home-based exercise (correction; low-load exercises). (n=52)	Radial extracorporeal shock-wave therapy (rESWT) by a PT (4-6 visits/4-6 weeks); low- to medium energy, frequency = 8-12 Hz, pressure = 2.5 to 4.0 bar, dose≥2000 pulses/session at insertion of supraspinatus tendon, dorsolaterally below acromion and maximum of 3 trigger points in	12 and 18 weeks; 1 year	<u>Primary outcome:</u> shoulder pain and disability (SPADI, 0-100) <u>Secondary outcomes</u>: pain at rest and activity (9-point Likert scale, 0 (no pain) to 9 (sever pain)), specific shoulder functioning (7-point Likert scale, 1 (easy) to 7 (impossible)), active ROM, return to work,	Difference in mean change (Multimodal Care - rESWT) <u>12 weeks</u> SPADI (0-100): 10.3 (95%CI 0.80, 19.80) <u>18 weeks</u> (SPADI (0-100): 8.4 (95%CI 0.60, 16.50) <u>1 year:</u> <u>SPADI (0-100): 7.6 (95% -0.50; 16.60)</u> No statistically significant differences in other secondary outcomes at any follow-up point.

			rotator cuff muscles. (n=52)		medication used. Adverse events	
Geraets et al., 2005 (86)	Adults (≥18y.o.), recruited by GP or advertisement from 2002 to 2003 in the Netherlands Case Definition: Shoulder complaints any region of the shoulder, periscapular, and arm region shaded area for ≥ 3 months. (n=176)	Multimodal care by a PT (≤18 group sessions over 12 weeks): Behavioural treatment program with graded activity, time contingency, and operant conditioning in group setting. Specific shoulder exercise: reaching, supporting, pushing, pulling, hitting, stabilizing, and work-related activities. (n=87)	Usual care by GP (12 weeks): Dutch College of General Practitioners Practice Guideline for Shoulder Complaints (1999): information; recommendations; pain-contingent medical or pharmaceutical therapy; wait and see policy (first two weeks. (n=89)	12 and 52 weeks	<u>Primary Outcomes:</u> Patient-specific complaints (Main Complaints Instrument, 0-100), shoulder disability (SDQ, 0-100) <u>Secondary Outcomes</u>: Perceived recovery (8-point ordinal scale, 0, fully recover, to 7, very much deteriorated), shoulder pain (Shoulder Pain Score), health-related quality of life (EuroQoL-5D, -1-1), catastrophizing and coping with pain (PCCL), kinesiophobia (TSK), fear avoidance beliefs (FABQ)	<u>Difference in mean change (Multimodal Care – Usual Care):</u> 12 weeks: Main complaints (0-100): 7.5 (95% CI 0.0; 15.0) SDQ (0-100): 1.7 (95% CI -5.4; 8.8) 52 weeks: Main complaints (0-100): 9.2 (95% CI 1.2; 17.3) SDQ (0-100): 2.1 (95% CI -6.5; 10.7) Perceived recovery: RR 1.8 (95% CI 1.0; 3.3)* No statistically significant differences in other secondary outcomes.
Ginn & Cohen, 2005 (87)	Adults (> 18 y.o.) recruited from a public hospital in Australia. Case Definition: unilateral pain (>1 month) over the shoulder joint and/or the proximal arm exacerbated by active shoulder movements. (n=138)	Multimodal care: 10 visits/5 weeks by a PT; interferential therapy, ultrasound, hot packs, ice packs, passive joint mobilization, daily ROM exercises. (n=42)	Exercise: Individualized daily home-based exercises supervised by PT 5 visits/5 weeks; stretching, strengthening. (n=48) Corticosteroid injection: Subacromial injection (40 mg methylprednisolone acetate); encouraged to use affected upper, provided by a rheumatologist. (n=48)	5 weeks	Hand-behind-back ROM: distance between T1 spinous process & the radial styloid process; unaffected side – affected side; Isometric strength (abduction): hand-held dynamometer; Self-rated improvement: 3-point Likert scale	<u>Multimodal care vs. Exercise:</u> No statistically significant difference for any outcomes. <u>Multimodal care vs. Corticosteroid injection:</u> No statistically significant difference for any outcomes

Haahr et al., 2005 & Haahr & Andersen, 2006 (88, 89)	Adults (18-55 y.o) referred to Herning Hospital, Denmark. Case Definition: subacromial impingement (6 months to 3 years). (n=84)	Multimodal care provided by a PT (19 visits/12 weeks): heat; cold pack; soft tissue treatment; exercise; home program. (n=43)	Surgery: subacromial decompression (bursectomy with partial resection of the antero-inferior part of the acromion and the coracoacromial ligament) followed by exercises provided by a PT (n=41)	3, 6 and 12 months	Primary Outcome: Constant-Murley Score, 0-100 (pain (VAS), limitations in activities of daily living (ADL); active range of motion (ROM) in 4 directions); shoulder strength Secondary Outcome; PRIM score (0-36), pain and discomfort (worst, average) (Likert scale; 0-9]	Difference in Mean Change Score (Multimodal Care – Surgery): Constant-Murley Score (0-100) 3 months: Pain: 0.3 (95% CI -1.31; 1.91)*; Function: 0.0 (95% CI -1.96; 1.96)*; ROM: 3.9 (95% CI -0.66; 8.46)*; Force: 0.3 (95% CI -1.86; 2.46)*; Total: 4.6 (95% CI -3.6; 12.8)* 6 months: Pain: -0.1 (95% CI -1.75; 1.55)*; Function: 0.9 (95% CI -1.36; 3.16)*; ROM: 0.7 (95% CI -4.0; 5.4)*; Force: -0.2 (95% CI -2.6; 2.2)*; Total: 1.4 (95% CI -8.01; 10.81)* 12 months: Pain: 0.1 (95% CI -1.52; 1.72)*; Function: 0.7 (95% CI -1.52; 2.92)*; ROM: 3.4 (95% CI -1.51; 8.31)*; Force: -0.1 (95% CI -2.74; 2.54)*; Total: 4.2 (95% CI -5.42; 13.83)*. No statistically significant differences for all other outcomes at any follow-up point.
Hay et al., 2003 (90)	Adults (≥18y.o.), recruited between 1998 to 2000 in the United Kingdom Case Definition: new episode of unilateral pain in shoulder region, including upper arm, elicited or exacerbated by active/passive movement (n=207)	Multimodal care by a PT (8 visits/ 6 weeks): Advice and instruction on pain relief and active shoulder exercises, reinforced by a home program ultrasound, manual therapy (n=103)	Corticosteroid injection by GP (1-2 injections): 40 mg of methylprednisolone mixed with 4 ml 1% lidocaine (lignocaine) into subacromial space. Advice to avoid overuse of shoulder for 48 hours and participants could return within 4 weeks for second injection if symptoms persisted. (n=104)	6 weeks	Primary outcomes: Shoulder disability (SDQ, 0-23) Secondary outcomes: Global assessment of change (5-point Likert scale, from "complete recovery" to "much worse"); pain severity (NRS, 1-10), impairment of function (NRS, 1-10), severity of main complaint (VAS, 0-10 cm) ROM	Difference in mean change (Multimodal care-Corticosteroid Injection): SDQ, 0-23 6 weeks: -0.5 (95% CI -2.1; 1.2) Patient global assessment (completely recovered + some improvement): 6 weeks: RR 1.09 (95% CI 0.93; 1.29)* Patient global assessment (completely recovered): 6 weeks: 0.33 (95% CI 0.14; 0.79)* No statistically significant differences for all other outcomes at any follow-up point.
Johansson et al.,	Adults (30-65 y.o) from primary care	Multimodal care by PT: 1) acupuncture (10	Corticosteroid injection (1 ml Depomedrone (40	6 weeks;	Primary outcome: pain and shoulder function	Difference in mean change (Multimodal care – Corticosteroid Injection):

2011(91)	centres, Sweden during 2004-2007. Case Definition: subacromial impingement syndrome pain (≥ 2 months) in deltoid area provoked by arm elevation, positive impingement tests. (n=123)	visits/5 weeks): standardized needle placement with 3 stimulations performed to achieve 'deqi' (immediately after needle insertion, 15 minutes, & 30 minutes) , and 2) 2-step home exercise program: part 1 –rotator cuff ROM; part 2 – strengthening (n=58)	mg methylprednisolone) + 8-10 ml of 1% prilocaine). Advice to refrain from heavy arm activities for 2 weeks provided by GP. A second injection was given if needed. (n=65)	3, and , 12 months	(AL-Score, 0-100); Secondary outcomes: Health Related QoL (EQ-5D: EQ-5D descriptive system, -1.0 to 1.0; and EQ-VAS, 0-100); global assessment of change (5-point Likert scale from "1=worse" to 5=recovered").	AL-Score 6 weeks: 0.0 (95% CI -3.5; 3.5)*; 3 months: -4.00 (95% CI -7.72; -0.28)*; 6 months: -6.00 (95% -9.82; -2.18)*; 12 months: -3.00 (95% -6.39; 0.39)* Global assessment of change (large improvement or recovered):6 months: Multimodal care: RR 1.46 (95% CI 1.03, 2.07) No statistically significant differences for all other outcomes at any follow-up point.
Rhon et al., 2014 (92)	Adults (18 to 65 y.o.) recruited from family practice and orthopedic clinics to a physical therapy department at a US military hospital-based outpatient clinic Case Definition: Unilateral shoulder pain (glenohumeral region) meeting diagnostic criteria for shoulder impingement (n=104)	Manual PT by PT (2 30-min sessions twice weekly/3 weeks): Combination of manual techniques to include joint mobilisations (both thrust and non-thrust techniques), soft-tissue mobilisations, manual stretches; contract-relax techniques, plus a home exercise program to reinforce clinic based intervention. (n=52)	Corticosteroid injection by GP (40 mg of triamcinolone acetonide). Handout explaining effects of steroid injection and how to manage flare-ups/pain, description of pendulum exercises. Maximum 3 injections (>1 month between injections) (n=52)	1, 3, 6, 12 months	Primary outcome: Shoulder Pain and Disability Index (SPADI, 0-100); Secondary outcomes: Patient's Global Rating of Change Scale (-7 to +7); Numeric Pain Rating Scale (NPRS, 0-10); shoulder-related health care use	(Manual PT – Corticosteroid injection) Difference in Mean Change Score: SPADI, 0-100 1 month: -0.10 (95% CI -5.15; 4.95)* 3 months: 2.70 (95% CI -2.41; 7.81)* 6 months:-0.40 (95% CI -5.48; 4.68)* 12 months: 0.40 (95% CI -4.59; 5.39)* NPRS, 0-10 1 month: 0.60 (95% CI 0.02; 1.18)* 3 months: 1.30 (95% CI 0.72; 1.88)* 6 months:1.00 (95% CI 0.43; 1.57)* 12 months: 0.90 (95% CI 0.33; 1.47)* Health Care Use (RR): Primary care provider visits after initial care: 0.64 (95% CI 0.43; 0.95) Needed any additional corticosteroid injection: 0.77 (95% CI 0.59; 0.99) Additional PT visits: 0.86 (95% CI 0.75; 1.04) Orthopedic surgeon visits: 1.24 (95% CI 0.71; 2.15) Plain radiography: 0.93 (95% CI 0.78; 1.11) Magnetic resonance imaging: 1.14 (95% CI 0.94; 1.38) Surgery: 1.01 (95% CI 0.93; 1.09)
Szczurko et al., 2009 (93)	Postal employees (18-65 y.o), from Canada.	Diet-based multimodal care provided by a naturopath	Exercise based multimodal care provided by a	12 weeks	Primary outcome: Shoulder pain and disability (SPADI, 0-	Difference in mean change: (Diet-based Multimodal care – Exercise based Multimodal care):

	Case Definition: pain in at least 1 shoulder (≥6 weeks), symptoms consistent with rotator cuff tendinitis. (n=89)	(12 visits/12 weeks); Needle acupuncture at pre-specified points (LI-15, SJ-14, SI-19, SI-10 to 13, BL-41 to 46, up to 4 tender points) with manual stimulation (duration of at least 10 minutes, at least 1 instance of restimulation); dietary advice (anti-inflammatory diet; fish, soybeans, cherries, berries, fruits, vegetables, nuts and whole grains, and decrease alcohol consumption); Phlogenzym supplement (2 tablets 3 times/day – 90 mg of bromeleain, 48 mg of trypsin and 100 mg of rutin) (n=45)	naturopath (12 visits/12 weeks); Passive, active-assisted, and active shoulder ROM exercises; hands-on shoulder muscle and joint therapy; placebo tablets (n=44)		100) <u>Secondary outcomes</u>: health-related quality of life (SF-36), patient specific outcome (MYMOP), ROM-flexion, extension, abduction, adduction, internal rotation, external rotation (goniometer/inclinometer)	SPADI, Total (0-100): 28.97 (95% CI 19.91; 38.03) * Pain (0-50): 13.01 (95% CI 9.5; 16.52) * Disability (0-80): 15.86 (95% CI 10.11; 21.61) * SF-36 PCS (0-100): -5.29 (95% CI -7.58; -3.00) * MCS (0-100): -9.51 (95% CI -12.16; -6.86) * Physical functioning (0-100): -11.42 (95% -17.81; -5.03) * Role physical (0-100): -16.15 (95% CI -22.72; -9.58) * Bodily pain (0-100): -15.83 (95% CI -20.94; -10.72) * General health (0-100): - 12.28 (95% CI -18.21; -6.35) * Vitality (0-100): -10.15 (95% CI -15.37; -4.93) * Social functioning (0-100): -10.36 (95% CI -16.66; -4.12) * Role emotional (0-100): -16.09 (95% CI -23.07; -9.11) * Mental health (0-100): -14.66 (95% CI -20.32; -9.0) * MYMOP Symptom 1: 0.63 (95% CI 0.18; 1.08)* Symptom 2: 1.68 (95% CI 1.25; 2.12)*

* Calculations completed by the OMTIMa group

ADL: activities of daily living; AL-score: Adolfsson-Lysholm shoulder assessment score; AQOL: Assessment of Quality of Life; DASH: Disabilities of the Arm, Shoulder and Hand Outcome Measure; EQ-5D: Euro QoL 5D-five dimension self-report questionnaire; EQ-VAS: EuroQoL Visual Analogue Scale; ER: External Rotation; FABQ: Fear-Avoidance Beliefs Questionnaire; GP: General Practitioner; GPE: Global Perceived Effect; IR: Internal Rotation; MCS: SF-36 Mental Component Scale; MTrP: Myofascial trigger points; MYMOP: Measure Yourself Medical Outcomes Profile; NRS: Numeric Rating Scale; NSAID: Non-steroidal anti-inflammatory drug; PCCL: Pain Coping and Cognition List; PCS: SF-36 Physical Component Scale; PROM: Passive range of motion; PT: Physical therapy; QoL: Quality of Life; ROM: Range of motion; SDQ: Shoulder Disability Questionnaire; SF-36: Short Form-36; SPADI: Shoulder Pain and Disability Scale; TSK: Tampa Scale for Kinesiophobia; US; ultrasound; VAS: Visual Analogue Scale; y.o: years old

Table 3: Combinations of Interventions in Multimodal Care for Soft Tissue Injuries of the Shoulder Reported in Scientifically Admissible Randomized Controlled Trials, 2003-2014[a‡]

					Acupuncture	Corticosteroid Injection	Dietary Changes		Education	Exercise			Manual Therapy	Medication	Passive Modalities					Psychological Intervention	Soft Tissue Therapy				Surgery
Condition	Author, Year	Treatment Provider	Number of Visits	Treatment Period (weeks)			Dietary Advice	Dietary Supplements		Endurance	Strengthening	Flexibility	Mobilisation		Heat/Cold	rESWT	Interferential Therapy	Ultrasound	Taping		Compression	Stroking/ strumming	Massage	Mobilisation	
Subacromial Impingement Syndrome of Persistent Duration	Bennell et al., 2010 (82)	PT ≈	10	10							✓	✓	✓						✓	✓			✓		
		PT ≈	10	10														✓≠							
	Engebretsen et al., 2009 & 2011(84, 85)	PT ≈	24 (max)	12 (max)						✓	✓												✓		
		PT ≈	4-6	4-6												✓									
	Haahr et al., 2005 & 2006 (88, 89)	PT ≈	19	12							✓				✓						✓¤				
		SX/PT ≈	3	6-8							✓														✓
Subacromial Impingement Syndrome of Variable Duration	Johansson et al., 2011(91)	PT ≈	10	5	✓						✓														
		GP ≈	1-2	1-5		✓																			
	Rhon et al., 2014 (92)	PT≈	6	3							✓	✓	✓											✓	
		GP ≈	3(max)	52		✓																			
Rotator Cuff Tendinitis of Variable Duration	Szczurko et al., 2009(93)	ND *	12	12	✓		✓	✓																	
		ND †	12	12				✓ ≠		✓	✓		✓¤								✓¤				
Non-Specific Shoulder Pain of Persistent Duration	Bron et al., 2011(83)	PT *	12 (max)	12					✓			✓			✓						✓	✓			
		PT †	0	0																					
	Geraets et al., 2005(86)	PT ≈	18 (max)	12							✓									✓					
		GP ≈	1-2	12					✓					✓											
Non-Specific Shoulder Pain of Variable	Ginn & Cohen, 2005 (87)	PT ≈	10	5								✓	✓		✓		✓	✓							
		PT ≈	5	5							✓	✓													
		RT ≈	1	5		✓																			
	Hay et al., 2003 (90)	PT ≈	8 (max)	6					✓		✓		✓¤					✓							

Duration		GP ≈	2 (max)	4		✓																		

Empty cells indicate that the intervention component was not provided in the treatment arm.

‡Table includes only modalities reported in scientifically admissible studies

Acronyms: rESWT: radial extracorporeal shock-wave therapy; PT: physical therapist; SX: surgeon; GP: general practitioner; ND: Naturopathic doctor; RT; Rheumatologist

*Superior multimodal programs of care; ≈Equivalent multimodal programs of care; †Inferior multimodal programs of care

¤ Technique not specified; ≠ sham/placebo treatment

Table 4: Risk of Bias for Accepted Randomized Controlled Trials based on Scottish Intercollegiate Guidelines Network Criteria (64)

Author, Year	Research Question	Random-ization	Conceal-ment	Blinding	Similarity at baseline	Difference between arms	Outcome measure-ment	Percent drop-out*	Intention to treat	Multiple sites
Bennell et al., 2010 (82)	Y	Y	Y	Y	Y	Y	Y	Week 11 Intervention: 2/59=2.4% Placebo: 0/61=0% Week 22 Intervention: 5/59=8.5% Placebo: 3/61=4.9%	Y	CS
Bron et al., 2011 (83)	Y	Y	Y	Y	Y	Y	Y	Post-intervention Physical therapy: 3/37=8.1% Wait List: 4/35=11.4%	Y	NA
Engebretsen et al. (2009) & Engebresten et al. (2011) (84, 85)	Y	Y	Y	Y	Y	Y	Y	Week 6 Supervised Exercise: 6/52=11.5% Radial extracorporeal shockwave therapy: 8/52= 15.4% Week 12 Supervised Exercise: 2/52=3.8% Radial extracorporeal shockwave therapy: 0/52=0% Week 18 Supervised Exercise: 2/52=2.8% Radial extracorporeal shockwave therapy: 2/52=2.8% 12 months Supervised Exercise: 3/52=5.8% Radial extracorporeal shockwave therapy: 4/52= 7.7%	Y	NA

Geraets et al., 2005 (86)	Y	Y	Y	Y	Y	CS	Y	Post-intervention Graded exercise therapy: 8/87 = 9.2% Usual care: 18/89 = 20.2%	Y	CS
Ginn & Cohen, 2005 (87)	Y	Y	CS	Y	Y	CS	N	5 weeks Injection group: 6.3% Exercise group: 10.4% Multiple physical modalities group: 7.1%	Y	NA
Haahr et al., 2005 & Haahr & Andersen, 2006 (88, 89)	Y	Y	Y	Y	N	CS	Y	12 months Physiotherapeutic training: 4.4% Arthroscopic subacromial decompression: 8.9% 4 years Physiotherapeutic training: 6.7% Arthroscopic subacromial decompression: 4.4%	Y	NA
Hay et al., 2003 (90)	Y	Y	Y	Y	Y	N	Y	6 weeks PT 4/103 = 3.9% Injection 6/104 = 5.8% 6 months PT 4/103 = 3.9% Injection 7/104 = 6.7%	Y	CS
Johansson et al., 2011(91)	Y	Y	Y	Y	CS	Y	Y	Post-intervention Subacromial corticosteroid injection 16/65=24.6% Acupuncture with home-exercises 16/58=27.6%	Y	CS
Rhon, Boyles and Cleland, 2014 (92)	Y	Y	Y	Y	N	CS	Y	1 month Corticosteroid injection: 6/52=11.5% Manual Physical Therapy: 4/52= 7.7% 3 months Corticosteroid injection: 7/52 = 13.5% Manual Physical Therapy: 8/52=15.4%	Y	NA

								6 months Corticosteroid injection: 7/52=13.5% Manual Physical Therapy: 7/52=13.5% 1 year Corticosteroid injection: 4/52=7.7% Manual Physical Therapy: 0/52=0.0%		
Szczurko et al., 2009 (93)	Y	Y	Y	Y	Y	CS	Y	Post-intervention Naturopathic care group: 20.9% Physical Exercise: 28.6%	Y	NA

*Percent drop-out incorporates both participant withdrawal and loss to follow-up.
Acronyms: Y: Yes; N: No; CS: Can't Say (insufficient detail to allow an assessment to be made); NA: Not Applicable; PT: Physiotherapy

Table 5: Risk of Bias for Scientifically Inadmissible Randomized Controlled Trials based on Scottish Intercollegiate Guideline Networks (SIGN) Criteria (64)

Author, Year	Research Question	Random-ization	Conceal-ment	Blinding	Similarity at baseline	Difference between arms	Outcome measure-ment	Percent drop-out*	Intention to treat	Multiple sites
Brox et al., 1993 & Brox et al., 1999 (94, 95)	Y	Y	N	Y	N	CS	CS	3 months Surgery: 14/45=31.1% Placebo: 3/30=10% Exercise: 8/50=16% 6 months Surgery: 4/41=8.9% Placebo: 0/30=0% Exercise: 1/50=2% 2 ½ years Surgery: 6/45=13.3% Placebo: 1/30=3.3% Exercise: 5/50=10%	Y	NA
Dickens et al., 2005 (53)	Y	Y	Y	Y	CS	CS	Y	6 months Physiotherapy: 3/45=6.7% Control:	Y	NA

								9/40=22.5%		
Melegati et al., 2000 (96)	Y	CS	CS	CS	CS	CS	CS	CS	CS	NA
Molsberger et al., 2010 (97)	Y	Y	Y	Y	Y	CS	Y	6 weeks Sham: 12/135=8.9% Verum: 11/154=7.1% COT: 41/135=30.4% 3 months Sham: 73/135=54.1% Verum: 37/154=24.0% COT: 70/135=51.6%	Y	CS
Winters et al., 1997 & 1999 (98, 99)	Y	CS	CS	Y	N	CS	CS	Manipulation: 19/32=59% Physiotherapy: 18/35=51% Corticosteroid injection: 7/47=15%	Y	CS

*Percent drop-out incorporates both participant withdrawal and loss to follow-up.
Acronyms: Y: Yes; N: No; CS: Can't Say (insufficient detail to allow an assessment to be made); NA: Not Applicable