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Evidence (-based medicine) in manual medicine/manual therapy—a summary review

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Abstract

Objective: The aim of this summary review is to analyse the current state of evidence in manual medicine or manual therapy.
Methods: The literature search focussed on systematic reviews listed in PubMed referring to manual medicine treatment until the beginning of 2022, limited to publications in English or German. The search concentrates on (1) manipulation, (2) mobilization, (3) functional/musculoskeletal and (4) fascia. The CASP Checklist for Systematic Reviews was used to present the included reviews in a clear way.
Results: A total of 67 publications were included and herewith five categories: low back pain, neck pain, extremities, temporomandibular disorders and additional effects. The results were grouped in accordance with study questions.
Conclusion: Based on the current systematic reviews, a general evidence-based medicine level III is available, with individual studies reaching level II or Ib. This allows manual medicine treatment or manual therapy to be used in a valid manner.

Keywords
Low back pain · Temporomandibular disorder · Neck pain · Extremities · Musculoskeletal

Background

In recent years, the European Scientific Society of Manual Medicine (ESSOMM) has developed "the European core curriculum and principles of manual medicine" (MM) [40]. Many authors from all of the member countries of ESSOMM have contributed substantially to the important issues. They state in their introduction: "The techniques and methods of manual medicine are diverse and innumerable, therefore, it was necessary to delineate the scientific background in anatomy and physiology on which they were based, to gather proof of their effectiveness in reported clinical studies and to identify the positioning of manual medicine in complex clinical therapeutic regimens" [40].

MM consists of "manual diagnostic examination of the locomotor system, the head and connective tissue structures and of manual techniques to treat reversible dysfunction and the pain associated with it aiming to prevention, cure and rehabilitation. Diagnostic and therapeutic procedures are based on scientific neurophysiological and biomechanical principles" [40].

The procedures described in this curriculum relate specifically to investigating and treating tension and pain in muscles, joints and connective tissues as well as structures located within these tissues. The main goal of the therapeutic techniques is to eliminate or reduce movement restrictions and pain.

In Germany, MM is practiced by doctors specialized in this field and as "manual therapy" (MT) by physical therapists (PT). In the United States of America, MM is taught and practiced by doctors of osteopathy (DO). The German Society of Manual Medicine (DGMM) considers osteopathy as a part and an extension of MM.

Supplementary Information

The online version of this article (https://doi.org/10.1007/s00337-022-00913-y) includes additional tables.

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Chiropractic, as a form of so-called complementary medicine, aims also on motor dysfunction and pain in the movement system. In the USA, osteopathy is taught at universities offering a DO degree. In Europe, MM is taught through non-academic seminars whose teachers and, to a large extent, their graduates are organized into national scientific societies. MT is also taught through schools run by professional physical therapy organizations. The criteria and rules for training and further education in MM and MT are specified and controlled by the medical association and the health insurance companies. In contrast, there are no such controlled rules for training in osteopathy and it is taught, learned and used by doctors, PT, and lay people alike. On this inconsistent basis, there are a variety of different textbooks, most of which were written by experienced users of MM. Greenman's book "Principles of Manual Medicine" can be considered as a basic textbook in MM, which received the title *Lehrbuch der osteopathischen Medizin* in the German translation [23, 24].

MM, MT and osteopathy are now widely used worldwide as proven conservative methods in the treatment of functional limitations and pain in the musculoskeletal system. However, the terms MM, osteopathy and MT are used inconsistently and promiscuously. This inconsistency is reflected by a wide spectrum in the different variables of clinical practice:

- Techniques for treatment are commonly described as *manipulation*, mostly as a thrust (impulse) with high velocity and low amplitude (HVLA technique); *mobilization*, as passive, mostly repeated movement by traction and/or rotation, e.g. joint mobilization; *soft tissue techniques* or *muscle energy techniques,* as massage-like techniques, e.g. "*strain–counter strain"* and others.
- The specific path and level of training and skills of the acting people, i.e. physicians, physical therapists, osteopaths, chiropractors, laymen.
- The spectrum of diagnosed and treated complaints and disorders:
  - Pain: low back pain (LBP), neck pain (NP), headache, muscle or joint pain.
  - Restricted spine or joint movement (hypomobility), hypermobility, elevated muscle tone.

In the past three decades, a growing number of case reports, retrospective analyses and randomized controlled trials (RCTs) have accumulated in the literature, which has also resulted in a greater number of published systematic reviews. The authors of these studies are looking for answers about the strength and effectiveness of their MM-based intervention. This is mostly done directly or in comparison versus an alternative treatment. The outcomes are discussed very differently. The focus is on the special conditions of the execution of the treatment in the context of study quality, as well as on the criteria for the statement about the evidence.

Because there have been a large number of reviews on this problem in recent years, it is our goal to analyse the current state of evidence in MM based on the available reviews regarding the varying influencing factors on the effects of MM and MT treatment. The aim of this summarizing review is to give an overview of the current state of evidence for hands-on techniques, independent of special techniques or localization of complaints.

Methods

The aim of this summarizing review is to gain a picture of the level of evidence in MM. For this purpose, a corresponding literature search was conducted in autumn 2019 using the PubMed database. In order to keep the review up to date, the literature search was repeated at the beginning of 2022. In this way, numerous reviews could be added.

The search strategy included various terms, which were divided into four categories:

- First category, manipulation: spinal manipulation OR manipulation thrust OR HVLA OR high-velocity low-amplitude OR HVT OR high-velocity thrust OR OMT OR osteopathic manipulative treatment OR manipulation with impulse OR musculoskeletal manipulation.
- Second category, mobilization: (mobilization OR mobilization) AND (manual OR joint OR spine OR extremity)
- Third category, functional/musculoskeletal: ("manual medicine" OR "manual therapy") and (functional OR musculoskeletal OR disorder)
- Fourth category, fascia: ("manual medicine" OR "manual therapy") AND (fascia OR myofascial OR neurofascial)

The search was limited to the last 10 years, to studies with humans and to full texts of clinical studies and reviews in German or English language.

First, the literature was narrowed down by title. The second step in the selection process was to review the available abstracts. Furthermore, only the reviews were extracted from this large number of hits, in order to avoid duplication of content that had already been summarized.

In addition, a free search was carried out on the topic of manual therapy in subject-specific databases of the Dutch manual medicine association and the *Ärztevereinigung Manuelle Medizin, Berlin*, whereby here, again, only reviews were included into the overview.

To sum up, publications were included if they address manual medicine or manual therapy treatment in an original manner and if they were presented as a systematic review. Studies were excluded if they concentrate on concomitant factors like cost effectiveness or topics other than therapy. Furthermore, single trials, conference papers and so on were ruled out.

Abbreviations

ANS	Autonomic nervous system
DGMM	German Society of Manual Medicine
EBM	Evidence-based medicine
ESSOMM	European Scientific Society of Manual Medicine
HVLA	High-velocity low-amplitude
LBP	Low back pain
MM	Manual medicine
MT	Manual therapy
NP	Neck pain
NRS	Numeric rating scale
OA	Osteoarthritis
OMT	Orthopaedic manual therapy
PPT	Pain pressure threshold
PT	Physical therapists
RCT	Randomized controlled trials
ROM	Range of motion
SMT	Spinal manipulative therapy
TMD	Temporomandibular disorder
TMJ	Temporomandibular joint
VAS	Visual analogue scale

Currently, there is no systematically developed reporting guideline for overviews [56]. The CASP Checklist for Systematic Reviews was used to present the studies found in a meaningful and clear way [7]. It must be emphasized that the aim of this checklist is not to evaluate the included research. Rather, the three sections of the CASP checklist support answering of the questions about validity, the results and the consequences that can be drawn for clinicians and researchers. Therefore, the referring tables can be found in the supplementary material.

Two reviewers extracted the data regarding target/treatment, the used assessments, the studies included and the found outcome. Furthermore, the CASP scale was used by both, to allow a better overview. Disagreements were resolved by a third opinion.

Results

Search results

With the chosen search strategy, 4720 hits were obtained in the specialist literature via the PubMed database and an additional free search. Screening the records by title and abstract left 378 hits. To concentrate on realistic and generally valid statements concerning the evidence of MM or MT, only the reviews were selected ($n = 88$). The published papers were assessed for eligibility, with a final number of 67 records; 21 reports had to be excluded for different reasons, e.g. topics other than therapy, focus on cost effectiveness or the small number of included studies, etc.

The remaining studies could be divided into five categories: 1) low back pain (LBP) with $n = 17$ reviews, neck pain (NP) with $n = 12$ reviews, extremities with $n = 11$ reviews, temporomandibular disorder (TMD) with $n = 8$ reviews and additional or other effects with $n = 19$ reviews. The literature search is illustrated in **Fig. 1**.

Low back pain

From the reviews found and selected, we classified 18 publications in the group "treatment of LBP with MM" [14, 18, 20–22, 26, 33, 34, 38, 39, 48, 50, 52, 59, 64, 65, 71, 72], where 11 of them described the treatment of unspecific LBP with HVLA [21], spinal manipulation [18, 33, 59] or spinal manipulative therapy (SMT) [50, 52, 59, 64, 65]. Other manual treatments are qualified as mobilization [14, 38, 59], manual therapy [20, 22, 39, 48] or other hands-on treatments, e.g. myofascial release or osteopathic manipulative treatment [48, 72]. The term "manual therapy" is inconsistently used for all hands-on interventions. Three reviews were targeted to MM in pregnancy-related LBP and pelvic pain [26, 71, 72], and one review to pain and disability caused by symptomatic lumbar spine stenosis [34].

Table 1 gives a summary of the treatment and intention of treatment, the assessments and included studies, and a summary of the results. Outcome in pain reduction is proved by a visual analogue scale (VAS) or numeric rating scale (NRS), functional enhancement by questionnaires such as the Oswestry Disability Questionnaire, Roland–Morris Disability Questionnaire or Short Form-36 Health Survey; occasionally by range of motion (ROM). The reviews that focused on non-specific LBP included up to 46 [20] studies, most more than 10 studies. One review has a summary of 6000 patients [59]. The quality of the studies evaluated in the reviews was not sufficient for meta-analysis, or meta-analysis could not include all studies from the review [65] because of deficits due to study quality.

The outcomes of SMT or MT are described as "to offer significant benefits in management of pain and function" [18, 33, 39, 52, 64], "to be better than usual medical care" as well as "short-term effects on pain relief and functional status" or significant benefit up to 6 weeks. One review with 26 RCTs and about 6000 participants in total [59] demonstrated high-quality evidence that spinal manipulation therapy in non-specific LBP has a statistically significant short-term effect on pain relief and functional status in comparison with other interventions. Evidence suggests that SMT causes neurophysiological effects (local hypoalgesia, sympathoexcitation, improved muscle function) [38, 50, 59]. Spinal manipulation in addition to general practitioner care was relatively cost effective [18, 20, 33]. The reviews support that "manipulative treatment should be part of musculoskeletal rehabilitation of LBP" [22].

No serious aversive events were reported.

Ten studies with 1198 pregnant women suffering from LBP and pelvic girdle pain report "limited evidence to support the use of MT on pain intensity as an option during pregnancy" [26, 72] whereas SMT "showed a significant effect on reducing pain in women with primary dysmenorrhea" [1], with the shortfall that not all studies reported dosage or session duration. Chiropractic care in postpartum LBP was not identified as a treatment option.

Studies in lumbar spine stenosis "showed better results in surgery for pain, disability and quality of life when continued conservative treatment has failed for 3 to 6 months" [34].

Hier steht eine Anzeige.

Neck pain

From the reviews found and selected, we classified 12 publications in the group "treatment of NP with MM" [11, 12, 16, 19, 25, 28, 30, 36, 47, 61, 75, 76]. NP is described as non-specific, mechanical or cervicogenic NP with or without headache or radicular findings. One review focused on cervicogenic dizziness treated with HVLA or mobilization [42]. **Table 2** gives a summary of the treatment and intention to treat, the assessments and included studies, and a summary of the results. Measurement of the results in pain reduction and functional improvement is by VAS, cervical ROM, NRS, neck pain questionnaire and/or dizziness handicap inventory. The 11 reviews that focused on NP included 3 to 23 studies.

Manual interventions consisted mostly of manipulation (with or without thrust), mobilization or myofascial techniques. The term "manual therapy" is inconsistently used for all hands-on interventions.

Two reviews including 23 RCTs with 680 patients with acute NP and 929 patients with chronic NP [28] and six studies with around 600 patients [61] stated positive effects for HVLA as statistically significant and clinically relevant improvements for pain and disability immediately and for up to 1 week to 6 months.

Two large reviews [25, 47], both from the same research group, included 1400 and 1900 patients. In their conclusions they state a "support for combined mobilization, manipulation and exercise for short-term pain reduction" and found "low-quality evidence suggesting manipulation, mobilization and exercise to produce greater long-term pain reduction compared to no treatment and low-quality evidence for improvement in function" [47] and concluded "moderate-quality evidence after cervical manipulation and mobilization for similar effects on pain, function and patient satisfaction at intermediate-term follow-up than in control group" [25]. These findings are congruent with the outcome of the other reviews [12, 16, 19, 30]. It is mentioned that "outcome is consistent with evidence from previous systematic reviews" [28]. A long-term follow-up with low-quality evidence shows a non-significant difference between spinal manipulative treatment and other manual therapies [16]. The treatment period is reported mostly up to several weeks and follow-up-until 1 year. No serious adverse events were reported.

There is "moderate evidence in a favourable direction to support the use of HVLA or mobilization for cervicogenic dizziness" [42].

Temporomandibular disorder

Eight of the reviews found belong to the category "treatment of temporomandibular (joint) disorder (TMD) with MM" [3, 6, 19, 29, 37, 43, 46, 69]. The symptoms to treat are also called orofacial (myogenous and arthrogenous) disorder, sometimes accompanied by headache or myofascial pain. The intention of treatment is referred to as "orofacial myofunctional therapy" in these reviews [29]. One review included treatment of cardiovascular performance with C5/C5 HVLA manipulation [19].

Table 3 summarizes the treatments and intention of treatment, the assessments, included studies and results. The results were evaluated by VAS, maximal mouth opening (MMO) and pain pressure threshold (PPT). The eight reviews comprise 95 studies with about 2000 patients. These reviews report mostly a high risk of bias.

The outcomes are shown as evidence of orthopaedic manual therapy (OMT) in correcting "dentofacial deformities when combined with orthodontic treatment" [6, 29, 37, 43], "greater MMO (high evidence) [6], pain (moderate evidence) and PPT, compared to a usual care group", "MT targeted to the cervical spine decreased pain and increased mouth ROM" [3, 19, 37] and "significant large effect on active mouth opening and on cervicogenic headaches" [43]. In subjects with hypertension, blood pressure seemed to decrease after cervical HVLA manipulation [19].

Upper and lower extremities

Eleven of the publications found were assignable to the category "treatment of pain and dysfunctions in upper or lower extremities with MM" [2, 5, 15, 27, 41, 45, 54, 55, 60, 67, 74]: three reviews focused on knee osteoarthritis (KOA) [60, 67, 74], one on plantar heel pain [55], one on lateral ankle sprains [41], two on thumb carpometacarpal osteoarthritis [5, 27] and three further reviews on shoulder or elbow [2, 54] or on MT for rotator cuff tendinopathy [15]. **Table 4** gives a summary of the treatments with the intention of treatment, the assessments, the included studies and the results. Outcome is measured with VAS or other NRS, ROM, and WOMAC for KOA, regional typical functional tests and/or electromyography. The reports on KOA are based on 32 studies with more than 1000 patients. MT is meant as technique with contact to the soft tissues, bones, and joints, often "individualized based on examination findings" [60]. Results of treatment are described as preliminary evidence: "manual therapy significantly relieves pain, significantly improves physical function for >4 weeks [74], specifically as an adjunct to another treatment and versus comparators of no treatment" [60]. Regarding the long-term benefits of MT, the research findings were inadequate for making safe and reliable conclusions [67].

For MT containing joint manipulation in glenohumeral cuff tendinopathy, a "small but statistically significant overall effect for pain reduction compared with a placebo or in addition to another intervention" could be reported [15], whereas spinal manipulation on shoulder and upper limb pain "is not as effective as local treatment in reducing upper limb pain".

For upper limb pain, the overall quality of evidence was very low; no strong recommendations can be made for the use of spinal manipulation (SM) in these patients [2]. In patients with lateral epicondylalgia, cervical HVLA manipulation resulted in increased pain-free handgrip [19].

The reviews on carpal tunnel syndrome or thumb carpometocarpal osteoarthritis showed a short-term improvement of function with pain relief when MT was combined with therapeutic exercise [5] and also better outcome when compared with electrotherapy [27].

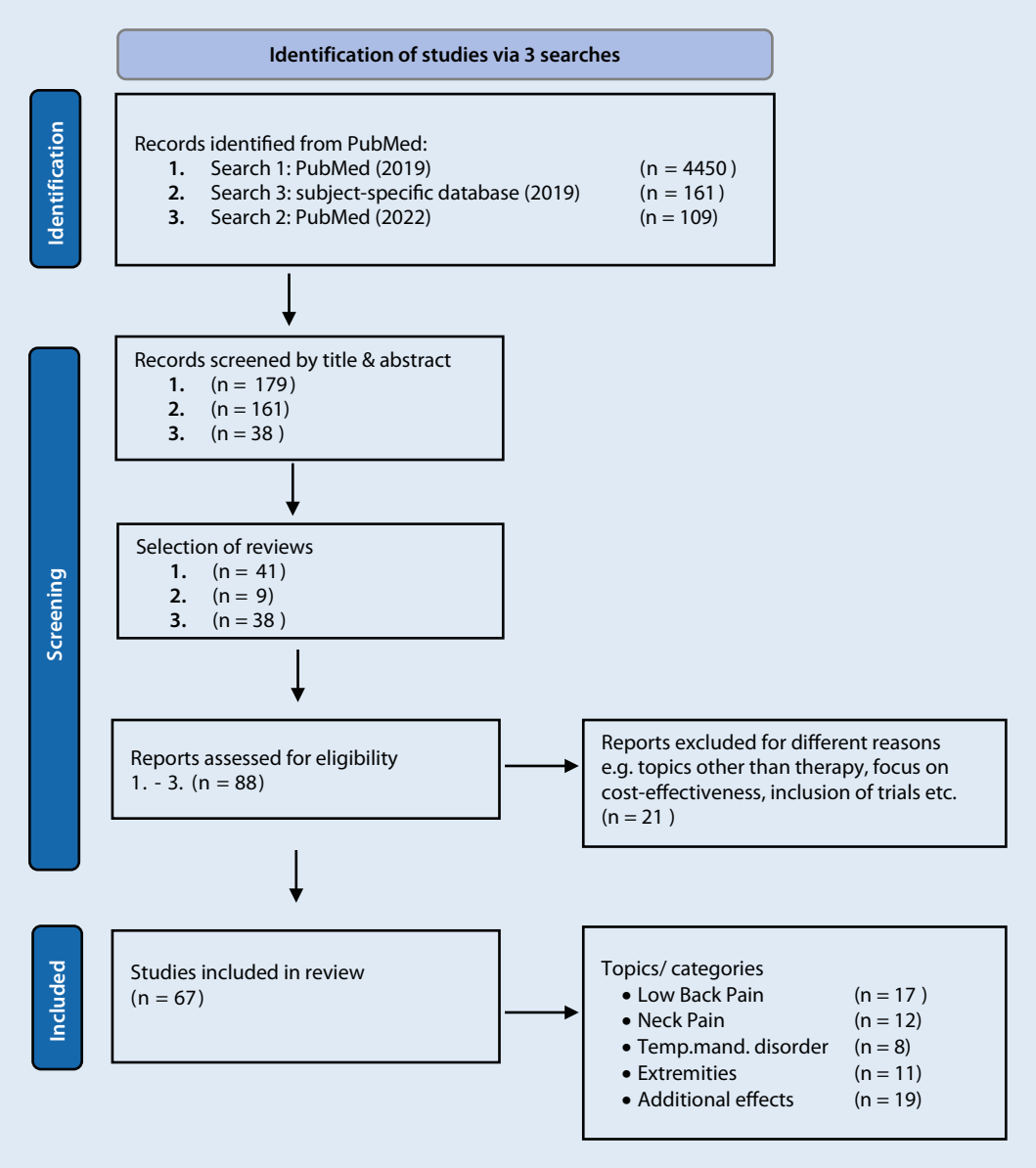

Fig. 1 ◄ PRISMA 2020 flow diagram for new systematic reviews. (From [51]

Additional effects of manual medicine treatment

Of the reviews found and selected, we classified 19 publications in the group of reviews searching for additional treatment effects after applying MM. Four reviews searched for changes in biochemical markers or for influence on the autonomic nervous system (ANS) after mobilization or MT [35, 49, 57, 58]. Outcome was measured with biochemical markers (neuropeptides, inflammatory and endocrine biomarkers from blood, urine or saliva) or via cardiovascular parameters, skin conductance or skin temperature. One reason that there are many studies referring to effects accompanying MM- and MT-induced pain relief and motor function improvement (>60) may be the insufficient knowledge about the mechanisms of MM treatment. On the other hand, the connections between pain, inflammatory activity and stress response suggest that changes triggered here can be measured—since pain itself is a subjective phenomenon.

Changes in cardiac parameters were expected when acting on the cervical or thoracic spine. Moderate-quality evidence on influencing biochemical markers is described, but was only followed up for a short time: modulation of pain and inflammation is possible, but without a statement on clinical importance [35] Results of OMT and MT are scarce in subjects, heterogeneous and limited in the methodological quality. No conclusive statement about influencing the ANS by cranial OMT can be reported, there may be responders and non-responders [57]. No declaration can be made on whether a certain treatment in an area can have more influence on the sympathetic or parasympathetic nervous system.

Two reviews focus on pelvic manual treatment. One shows significant evidence of pain reduction in primary dysmenorrhea [1]. The results of the second review including 18 studies might not necessarily apply to sustained application of external pelvic compression [4].

Table 1 Systematic reviews concerning low back pain

Author	Target/treatment	Assessment	Studies included/comments	Outcome
Dal Farra F et al. [14]	To assess effectiveness of osteopathic interventions in the management of NS-CLBP for pain and functional status. OMT, myofascial release, craniosacral treatment	All the included trials assessed pain levels and functional status, considered as the primary outcomes in the current review; VAS, Oswestry, mobility	*N* = 12 studies (1055 participants) – 6 studies osteopathic manipulative treatment	Osteopathic intervention effects results statistically significant in six trials. Results confirms and strengthen evidence that osteopathy improves pain levels and functional status in patients with NS-CLBP over a short-term period. MFR approach reported better levels of evidence for pain improvement if compared to other osteopathic modalities
Furlan AD et al. (2012) [18]	To evaluate the efficacy, harms and costs of the most common CAM treatments (acupuncture, massage, spinal manipulation and mobilization) for neck/low-back pain	VAS, Pain Disability Index, Oswestry Index, von Korf, Roland–Morris Disability Score	– 81 included in LBP (31 manipul/mob) – 52 included in NP (19 manipul/mob) – 13 studies manipulation alone	In older subjects with mixed LBP duration, spinal manipulation was significantly better than medical care or exercise in reducing disability at intermediate- and long-term follow-up. Spinal manipulation in addition to general practitioner care was relatively cost effective
Gianola S et al. (2022) [20]	To assess the effectiveness of interventions for acute and subacute non-specific LBP	Pain and disability outcomes	*N* = 46 for pain; 31 for disability 12 of them MT MT = e.g. spinal manipulation, mobilization, trigger points or any other technique	With uncertainty of evidence, NS-LBP should be managed with non-pharmacological treatments which seem to mitigate pain and disability at immediate term
Goertz CM et al. [21]	To evaluate patient-centred outcomes following a specific type of commonly used SM, high-velocity low-amplitude (HVLA), in patients with LBP	VAS, NRS, Roland-Morris, Oswestry The majority of studies included both pain and function as primary and/or secondary outcomes	*N* = 38 studies – 20 were evaluated for quality in one or more other reviews	Spinal manipulation for LBP shows a small but consistent treatment effect at least as large as that seen in other conservative methods of care
Gomes-Neto M et al. (2017) [22]	To examine the efficacy of stabilization exercises versus general exercises or manual therapy in patients with low back pain	VAS, NRS, disability and function assessed by any questionnaire	*N* = 11 studies (478 patients) Treatments 1–3/week 20–60 min, duration 4–36 weeks	MT was as efficacious as stabilization exercises in decreasing pain and disability and should be part of musculoskeletal rehabilitation for LBP
Hall H et al. [26]	To critically appraise and synthesize the best available evidence regarding the effectiveness of MT for managing pregnancy-related LBP and pelvic pain	LBP or pelvic girth pain intensity. Secondary outcomes included pain-related disability, quality of life, medication, acceptance and safety of women and children	*N* = 10 studies (1198 pregnant women)	Limited evidence to support the use of complementary manual therapies regarding pain intensity when compared to usual care and relaxation as an option for managing low back and pelvic pain during pregnancy; No difference to sham therapy
Kolber MR et al. [33]	To assess the benefit and harms of pharmacologic and nonpharmacologic therapies used in the management of chronic radicular or non-radicular LBP	Not reported	*N* = 18 RCTs (2561 patients followed for 6 to 52 weeks) SMT: 5 RCTs with 686 patients followed for 2 to 12 weeks were included Rubefacients (capsaicin only): 3 RCTs with 611 patients Acupuncture: 8 RCTs with 4618 patients followed for 4 to 24 weeks	SMT: low evidence, one trial did not find sustained benefit 42 weeks after SMT completion
Kovacs FM et al. [34]	To review the evidence on the effectiveness and safety of any form of surgery vs. conservative treatment for symptomatic lumbar spinal stenosis	Oswestry, SF-36	*N* = 11 studies (918 patients) 1–2–3–6 months Each care provider decided the form of conservative or surgical treatment	In all the studies, surgery showed better results for pain, disability and quality of life, although not for walking ability (more effective than continued conservative treatment when the latter has failed for 3–6 months)

Table 1 (Continued)

Author	Target/treatment	Assessment	Studies included/comments	Outcome
Lascurain-Aguirrebena I et al. [38]	To review evidence for mechanisms of action of spinal mobilizations	Surface EMG, muscle cross-sectional area, endurance and strength, ROM, stiffness, pressure and thermal pain threshold, posture sway index, pain at rest	*N* = 24 studies; (> 500 patients) First systematic review with a full analysis of the evidence for the mechanisms of action of spinal mobilizations	Evidence suggests that spinal mobilizations cause neurophysiological effects: hypoalgesia, sympathoexcitation and improved muscle function. Three of four studies reported reduction in spinal stiffness
Lavazza C et al. [39]	To assess effects and reliability of sham procedures in MT: hand contact sham treatment compared with MT (physiotherapy, chiropractic, osteopathy, massage, kinesiology and reflexology) in lumbar and cervical region	Primary outcomes were pain intensity	*N* = 24 (19 qualitative/2019 participants) SM/chiropractic: *n* = 7 studies (567 participants) Osteopathy (5 trials, 645 participants) Kinesiology (1 trial, 58 participants) Articular mobilizations (6 trials, 445 participants) Muscular release (5 trials, 304 participants) Symptom duration not reported	Very low evidence quality suggests clinically insignificant pain improvement in favour of MT compared with ST; similar effects were found with no treatment. The heterogeneousness of sham MT studies and the very low quality of evidence render uncertain these review findings. When blinding was ensured the effects of sham therapy and MT were larger
Namnaqani FI et al. [48]	To assess the effectiveness of the McKenzie method compared to manual therapy in the management of patients with chronic LBP	VAS, Oswestry, Roland–Morris, after 3, 6, 12 months	*N* = 5, no meta-analysis	In patients with CLBP, many pain measures showed that the McKenzie method is a successful treatment to decrease pain in the short term, while the disability measures determined that the McKenzie method is better in enhancing function in the long term
Nim CG et al. (2021) [50]	To explore whether SMT applied at a candidate site is superior to SMT applied at a non-candidate site in relation to the clinical outcome. Cervical pain (*n* = 6) Lumbar pain (*n* = 4)	Pain intensity or disability. Secondary outcomes included objective measurements, e.g. pressure pain detection threshold (PPT) and range of motion	*N* = 9 + 1 (944 patients); 4 reported funding SMT at the candidate site compared to SMT to the opposite side of the indication (i.e. at the same spinal level but on the contralateral side—"same level") SMT at the candidate site compared to SMT elsewhere in the same spinal region (i.e. cervical, thoracic or lumbar—"same region") SMT at the candidate site compared to SMT to a distant spinal region	None of these nine studies detected any statistically significant differences in the outcome measurements for the two treatment approaches: SMT given at a clinician-determined "correct" vertebral level did not have better outcomes than treatment given more haphazardly. Not retested if patients recognized that SMT was applied at the non-candidate site. Reasons for findings: *The candidate site is a subjective concept* *The manipulation is not specific* *A neuromuscular or biomechanical mechanism might explain the positive results of SMT* Some positive effects of SMT may be due to non-specific mechanisms
Paige NM et al. [52]	Is the use of SMT in the management of acute (≤ 6 weeks) LBP associated with improvements in pain or function? SMT was given alone or as part of a package of therapies	VAS, NRS Roland–Morris, Oswestry	*N* = 15 RCT (1711 patients) Heterogeneity was not explained	SMT treatments for acute LBP were associated with statistically significant benefit in pain and function at up to 6 weeks, which was, on average, clinically modest
Rubinstein SM et al. [59]	To assess the effects of SMT for chronic low-back pain; HVLA	VAS, NRS, Roland–Morris, Oswestry, SF-36, functional state, return to work	*N* = 26 RCTs (total participants = 6070), 9 of which had a low risk of bias Approximately two thirds of the included studies (*N* = 18) were not evaluated in the previous review	In general, there is high-quality evidence that SMT has a statistically significant short-term effect on pain relief and functional status in comparison with other interventions. Evidence suggests that SMT causes neurophysiological effects (local hypoalgesia, sympathoexcitation, improved muscle function)

Table 1 (Continued)

Author	Target/treatment	Assessment	Studies included/comments	Outcome
Thornton JS et al. (2021) [65]	To summarise the evidence for non-pharmacological management of LBP in athletes; spinal manipulation means mobilization (!)	VAS, SF-36, Oswestry, Roland–Morris, others including muscle strength	*n* = 14, 4 in meta-analysis 5 with MT (157 patients)	There were short-term beneficial effects of massage and spinal manipulation Acute LBP: spinal manipulations combined with icing and stretching improved pain by an average of 2 points (VAS 0–10) 24 h after one treatment
Weiss CA (1) et al. [71]	To assess effectiveness of chiropractic care options commonly used for pregnancy-related LBP, pelvic girdle pain (PGP) Osteopathic manipulative treatment	Self-reported changes in pain or disability	*N* = 50 studies, pregnancy Postpartum *n* = 16 studies 2 SRs of high and acceptable quality with 1 RCT each that examined OMT as part of a plan of management for managing LBP or PGP	Both SRs reported improvements in pain and disability with OMT as a treatment modality. Moderate, favourable evidence for electrotherapy and osteopathic manipulative therapy
Weiss CA (2) et al. [72]	To assess the effectiveness of specific chiropractic care options commonly used for postpartum LBP, pelvic girdle pain (PGP), or combination	Self-reported changes in pain or disability self-reported outcomes	*N* = 16; 5 SR, 10 RCT, 1 cohort study	No treatment option was identified as having sufficient evidence to make a clear recommendation

CAM complementary alternative medicine, *EMG* electromyography, *HVLA* high-velocity low-amplitude thrust, *LBP* low back pain, *MFR* myofascial release, *MT* manual therapy, *NP* neck pain, *NRS* numeric rating scale, *NS-CLBP* non-specific chronic LBP, *OMT* osteopathic manipulative treatment, *PGP* pelvic girdle pain, *SR* systematic review; *ST* sham treatment, *SF-36* short form-36 questionnaire, *SM/SMT* spinal manipulation /therapy, *RCT* randomized controlled trial, *SMT* spinal manipulative therapy

Two reviews show significant treatment effects of myofascial techniques on ROM and pain [70] and reduction of tender points [73].

One review found preliminary evidence supporting the effectiveness of subgroup-specific manual therapy in LBP, mostly in the short-term range [63].

Two reviews looked for the effect of manipulation and MT on vertigo and unsteadiness. 31 studies used balance tests, stabilography and a dizziness handicap inventory. The results show no correlation between pain reduction and stability, which limits the ability to generalize [32, 66].

Few studies are devoted to fibromyalgia [62, 68]. They are heterogeneous and usually only examine short-term effects. Results are insufficient to support and recommend the use of manual therapy.

One review (five studies) reports a positive effect on upper limbs and the thorax of female breast cancer survivors. MT decreased chronic musculoskeletal pain intensity and increased pain pressure threshold [13].

Nine studies focused on the effects of MT on the diaphragm. An immediate significant short-term effect on parameters related to costal, spinal and posterior muscle chain mobility could be shown [17].

Manual therapy is not significantly different to no treatment in terms of reducing fear-avoidance in individuals with chronic musculoskeletal pain [31].

No clinical studies support or refute the efficacy or effectiveness of SMT in preventing the development of infectious disease or improving disease-specific outcomes [8].

To date, there is no evidence for an effect of SMT in the management of non-musculoskeletal disorders including infantile colic, childhood asthma, hypertension, primary dysmenorrhea and migraine [10].

There are no studies measuring the incidence or association of cervical spine manipulation and internal carotid artery dissection [9]. **Table 5** summarizes the treatments and intention of treatment, the assessments, included studies and results.

Manual medicine treatments, especially myofascial techniques, are common and effective in a variety of complaints, e.g. in conditions after breast cancer or with fibromyalgia, dysmenorrhea, migraine, hypertension, infantile colitis, asthma or balance disorders—MM does not prevent their occurrence, but is helpful and facilitates in the management of several diseases.

Manual therapy influences the range of motion, pain intensity, flexibility and parts of the autonomic nervous system.

However, the level of heterogeneity between studies concerning intervention, outcome measures, comparison groups and implementation makes it difficult to draw consistent conclusions and give binding recommendations.

Diversity of research objectives

It is the aim of this summarizing review to evaluate the level of evidence for treatment with specific methods of MM for pain and functional disorders in the musculoskeletal system. The distribution of the keywords used for the search strategy describing the content of the evaluated literature is shown in **Fig. 2**. Manipulation and mobilization give 45%, MT results in 25%, and other manual or non-manual techniques add up to 30% of the keywords. Paying attention to the fact that the included reviews were published in about 30 different journals, these results speak for different intentions and aims of the single reviews. This is underlined by

Table 2 Systematic reviews concerning neck pain

Author	Target/treatment	Assessment	Studies included/ comments	Outcome
Cross KM et al. [11]	To assess effects of thoracic spine thrust manipulation (supine or seated thrust) on pain, ROM and self-reported function in patients with mechanical neck pain	VAS, faces pain scale; NDI, NPQ, NPRS, ROM	*N* = 6 reviews (limited number of RCTs)	Results indicate that thoracic spine thrust manipulation can provide a positive treatment effect immediately following thrust manipulation for up to 6 months
Cumplido-Trasmonte C et al. (2021) [12]	To determine the effectiveness of manual and non-invasive therapies in the treatment of patients only with tension-type headache; MT, global manipulation soft tissue technics	HIT-6, HDI, VAS, CROM, headache diary	*N* = 10 (19–42 patients) 4 studies MT; dose of MT was very heterogeneous	All the studies analysed show positive results in patients receiving physiotherapy with MT on pain intensity, pain frequency, disability, overall impact, quality of life, and craniocervical ROM in adults with tension-type headache. No clear evidence that any technique is superior to another
Fernandez M et al. [16]	To evaluate the effectiveness of SMT for CGHA	VAS, NRS, NDI, Headache Impact Test (HIT-6), mean headache hours per day, per week	*N* = 7 (> 600 patients)	Low-quality evidence showing a significant, small effect favouring SMT over other MT for pain intensity and disability; moderate-quality evidence for pain frequency. At long-term follow-up: low-quality evidence showing a non-significant difference between SMT and other MT for pain intensity (2 studies)
Gross A et al. [25]	To assess if manipulation or mobilization improves pain, function/disability, patient satisfaction and quality of life in adults experiencing NP with or without headache	Pain relief, function, disability and patient satisfaction; pain relief, and global perceived effect	*N* = 17 for meta-analysis	Moderate-quality evidence showed cervical manipulation and mobilization produced similar effects on pain, function and patient satisfaction at intermediate-term follow-up. Low-quality evidence suggested cervical manipulation may provide greater short-term pain relief than a control
Hidalgo B et al. [28]	To update the evidence for different forms of manual therapy and exercise for patients with different stages of non-specific neck pain. HVLA, mobilization, combination of both, other treatment	VAS, NPRS, NDI, CROM, overall health and quality of life; for short, intermediate-term, long-term (1 year)	*N* = 23 RCT (680 patients acute NP; 929 patients chronic NP)	HVLA with statistically significant and clinically relevant improvements for pain and disability from 1 week to 6 months. Moderate to strong evidence in favour of HVLA or combined HVLA and mobilization combined with exercise for improvement in pain, function and satisfaction; mobilization need not be applied at the symptomatic levels
Jin X et al. (2021) [30]	To evaluate the evidence pertaining to the efficiency and safety of using MT to treat patients with cervicogenic cephalic syndrome; MR, MT, acupuncture, exercise	VAS, Dizziness Handicap Inventory (DHI), NDI, ROM	8 RCTs (395 patients) meta-analysis No serious adverse effects	Significantly reduced scores of VAS, DHI and NDI. and improved ROM of the cervical spine
Kroll LS et al. (2021) [36]	To review the evidence for manual joint mobilization techniques (MR, MT), supervised physical activity, psychological treatment, acupuncture and patient education as treatments for TTH on the effect of headache frequency and quality of life	Headache frequency and intensity	*N* = 13 RCTs, 6 joint mobilization (MR technique, MT, osteopathic MT, suboccipital muscle manipulation)	Some positive effects were shown on headache frequency, quality of life, pain intensity and stress symptoms. Weak recommendation for joint mobilization

Table 2 (Continued)

Author	Target/treatment	Assessment	Studies included/ comments	Outcome
Lystad RP et al. [42]	To evaluate the evidence for MT in conjunction with or without vestibular rehabilitation in the management of cervicogenic dizziness	Dizziness frequency, dizziness intensity, posturography, VAS	*N* = 15 (5 RCTs), (592 patients)	12, including all five RCTs, reported improvements in dizziness and associated symptoms (e.g. neck pain) following MT. The remaining study measured skull spatial offset repositioning ability and found a significant improvement following soft tissue manipulation
Miller J et al. [47]	To assess if MT, including manipulation or mobilization, combined with exercise improves pain, function, disability, quality of life, global perceived effect and patient satisfaction for adults with NP with or without CGHA or radiculopathy	VAS, Northwick Park NP Questionnaire, Function and disability, quality of life, costs	*N* = 17 RCT multimodal treatment of neck pain: acute, subacute, chronic and mixed duration (5 whiplash associated, 1 degenerative changes, 5 cervicogenic headache, 3 radicular singes) 7 manipulation 5 mobilization 5 man & mob combination	Results favoured manipulation, mobilization and exercise over exercise alone, also for long-term pain reduction Moderate evidence favouring reduced costs consisting of MT and exercise Serious adverse events such as stokes or serious neurological deficit could not be established Various combinations of MT and exercise emerged to treat neck pain
Schroeder J et al. [61]	To compare manipulation or mobilization of the cervical spine to physical therapy or exercise for symptom improvement in patients with neck pain Cervical SM (chiropractic therapy), cervical spinal mobilization (MT)	ROM, VAS, disability SF-36, patient-rated treatment improvement, treatment satisfaction, health status	*N* = 6 studies (> 500 patients) No studies were performed in patients with chronic pain	Subjects who underwent mobilization therapy compared with physical therapy reported a greater improvement in general health at 7 weeks No differences in SF-36 between SM and home exercise at 12 or 52 weeks Low evidence in acute pain and functional improvement for SMT vs. exercise
Young JL et al. [75]	To evaluate the effectiveness of thoracic manipulation versus mobilization in patients with mechanical neck pain	VAS, CROM, disability scales	*N* = 14 studies (250 subjects in experimental group)	Significant amount of evidence, although of varied quality, for the short-term benefits of thoracic manipulation in treating patients with mechanical neck pain
Zhu L et al. (2016) [76]	To assess effects of cervical manipulation compared with no treatment, placebo or conventional therapies on pain measurement in patients with degenerative cervical radiculopathy	VAS, syndromes in TCM	*N* = 3 trials (502 participants) Each systematic review included a variety of conservative interventions or complex interventions	Above all, cervical SM showed significant immediate effects in improving pain scores compared with cervical computer traction. Long-term effects of cervical rotational manipulation were not observed

CGHA cervicogenic headache, *CROM* cervical range of motion, *DHI* dizziness handicap inventory, *HIT-6* Headache Impact *Test, HVLA* high-velocity low-amplitude thrust, *MT* manual therapy, *MR* myofascial release, *SM* spinal manipulation, *NDI* neck disability index, *NP* neck pain, *NPQ* Northwick Park Neck Pain Questionnaire; *NPRS* numeric pain rating scale, *RCT* randomized controlled trial, *ROM* range of motion, *SMT* spinal manipulative therapy, *TMC* traditional Chinese medicine, *TTH* tension-type headache, *VAS* visual analogue scale

an even broader spread in the so-called clearly focused questions targeted to different complaints: LBP and NP together result in 44%, extremity pain is about 16% and TMD adds up to 12% of the questions. Other targets are fascia, muscles, vegetative or physiological effects, as shown in **Fig. 3**.

Discussion

The quality of the studies integrated into a review is based on proven criteria for assessing a risk of bias. The weakest points in almost all studies are blinding of patients and care providers (treating person, outcome-assessors) and selective reporting. Not all studies reported session duration of treatments [26]. Cross et al. (2011) stated "it is impossible to blind the care provider in manual treatments and, when self-reported measures are used, the trials do not meet the observer blinding criteria" [11]. Only a few trials avoided co-intervention [11]. One criterion, which upgrades the body of evidence, is a large amplitude of effects. An overall strength of "high" means we have high confidence that the evidence reflects the true effect and further research is very unlikely to change our confidence in the estimation of the effect [64]. Quality decreases by inadequate execution and reporting, by the

Table 3 Systematic reviews concerning temporomandibular disorders

Author	Target/treatment	Assessment	Studies included/comments	Outcome
Armijo-Olivo S et al. (2016) [3]	To summarize evidence from and evaluate the methodological quality of randomized controlled trials that examined the effectiveness of MT and therapeutic exercise interventions in TMD	VAS, MMO, PPT	*N* = 48 studies (*n* = 40–130 treated persons/study) Unclear or high risk of bias	MT alone or in combination with exercises shows promising effects. MT targeted to the cervical spine decreased pain and increased mouth ROM in patients with myogenous TMD
Calixtre LB et al. [6]	To synthesize evidence regarding the isolated effect of MT in improving TMJ function, considering MMO and pain as main outcomes	Pain VAS, MMO, PPT	*N* = 8 studies (*n* = 374 patients) Most of the RCTs included were high methodological-quality studies	MT showed greater MMO (high evidence), pain (moderate evidence) and PPT compared to a usual care group
De Melo LA et al. (2020) [46]	To evaluate the effectiveness of MT in the treatment of myofascial pain related to TMD; several types of MT	Perception of subjective pain	*N* = 5 studies, (279 total patients) 156 were treated with MT only or MT with counselling	MT was better than no treatment in one study and better than counselling in another study; however, MT combined with counselling was not statistically better than counselling alone; MT alone was not better than botulinum toxin. MT combined with home therapy was better than home therapy alone in one study
Galindez-Ibarbengoetxea G et al. [19]	To describe the effects of cervical HVLA manipulation techniques on range of motion, strength, and cardiovascular performance	Perception of subjective pain	*N* = 11 studies (553 patients)	Cervical HVLA manipulation results in improvements in mobility as well as in the cardiovascular system. A large effect size was found in CROM improvement, especially for patients with neck pain. Rotation was the most clearly improved movement. In addition, mouth opening without pain was improved after upper cervical HVLA manipulation, mainly in patients with neck pain
Homem MA et al. [29]	To determine the existence of scientific evidence demonstrating the effectiveness of OMT as an adjuvant to orthodontic treatment in individuals with orofacial disorders	Functional parameters, Payne test, homogeneity test, cephalometric analysis, ultrasound of masseter	*N* = 4 RCT (212 patients) All papers had a high risk of bias; results quite particular to specific conditions: anterior open bite, orofacial dyskinesia, masseter thickness	Scientific evidence of orofacial MT in correcting dentofacial deformities when combined with orthodontic treatment
La Touche R et al. [37]	To assess the effectiveness of cervical MT on patients with TMD and to compare cervicocraniomandibular MT vs. cervical MT	VAS, MMO, pain pressure test, NDI	*N* = 6 studies; 5 for meta-analysis; (252 patients)	Cervical MT vs. other nonmanual therapy: all four included studies showed significant improvements in pain intensity Cervical MT vs. cervicocraniomandibular MT: significant reductions in pain intensity at 3 months of follow-up
Martins WR et al. [43]	To assess the effectiveness of a musculoskeletal manual approach in temporomandibular joint disorder patients	Active and passive MMO, mandibular movement, VAS, PPT, EMG on masseter muscle	*N* = 8 studies, (*n* = 160 patients)	Significant large effect on active mouth opening and on pain during active mouth opening in favour of musculoskeletal MT techniques when compared to other conservative treatments; beneficial effects with cervicogenic headaches
Van der Meer HA et al. [69]	To evaluate the literature on the effectiveness of physical therapy (exercise, orofacial MT, cervical MT) on concomitant headache pain intensity in patients with TMD	VAS	*N* = 5 studies, (107 patients)	Very low certainty that there is an effect of physical therapy for TMD on concomitant headache intensity

CROM cervical range of motion, *EMG* electromyogram, *HVLA* high-velocity low-amplitude thrust, *MMO* maximum mouth opening, *MT* manual therapy, *MTD* temporomandibular disorders, *NDI* neck disability index, *OMT* orofacial myofunctional therapy, *PPT* pressure pain threshold, *RCT* randomized controlled trials, *TMJ* temporomandibular joint, *VAS* visual analogue scale

Table 4 Systematic reviews concerning upper and lower extremities

Author	Target/treatment	Assessment	Studies included/comments	Outcome
Aoyagi M et al. [2]	To assess the effectiveness of SM in patients with upper limb pain as part of the concept of regional interdependence	ROM, NPRS, PPT, HPT (hot pain threshold), CPT (cold pain threshold)	*N* = 6 studies (201 patients), 3 for meta-analysis	Meta-analysis results suggested there were no statistical differences between SM and other interventions in terms of effects on reducing upper limb pain. The overall quality of evidence was very low; no strong recommendations can be made for the use of SM in these patients
Bertozzi L et al. (2015) [5]	To assess the effect of conservative interventions (exercise, MT) on pain and function in people with thumb carpometacarpal OA	Hand pain, hand physical function or other secondary measures of hand impairment such as grip or pinch strength, ROM or stiffness	*N* = 13 RCT, meta-analysis Follow-up to 12 months MT = 4 studies vs. control	Moderate-quality evidence that MT and therapeutic exercise combined with MT improve pain in thumb carpometacarpal OA at short- and intermediate-term follow-up
Desjardins-Charbonneau A et al. [15]	To search for efficacy of MT for rotator cuff tendinopathy	Pain at rest, VAS, ROM, NPRS	*N* = 21 studies (*n* = 880) Only 5 studies had a moderate to low risk of bias	Small but statistically significant overall effect for pain reduction of MT (low- to moderate-quality evidence) compared with a placebo or in addition to another intervention
Hernandez-Secorun M et al. [27]	To evaluate the effectiveness of conservative treatment (pharmacology, electrotherapy and MT) in patients with CTS regardless of the level of severity and the presence of systemic diseases	VAS, BCTQ (Boston Carpal Tunnel Questionnaire), BCTQ-SSS (BCTQ Symptom Severity Scale), BCTQ-FSS: (BCTQ Function Severity Scale), EMG-CMAP—several parameters	*N* = 29 studies (30–181 patients)	MT could be effective for severe CTS patients with a systemic condition in the short term The studies that compared MT and electrotherapy found significant differences in favour of the MT group
Loudon JK et al. [41]	To summarise the effectiveness of manual joint techniques in treatment of lateral ankle sprains	VAS, ROM, gait parameter	*N* = 8 studies (144 patients) Immediate effects	For treatment of subacute/chronic lateral ankle sprains, some form of joint MT appears to help with ankle ROM, especially dorsiflexion and pain reduction
Maxwell CM et al. [45]	To synthesize the effects of SMT on lower limb neurodynamics	Passive straight leg raise or slump test	*N* = 8 RCT 4 studies, SMT in thoracic and lumbar region	Limited evidence suggests SMT-improved range of motion and was more effective than some other interventions Comparisons of SMT to sham interventions were mixed
Pieters L et al. (2020) [54]	To evaluate the effectiveness of interventions within the scope of physical therapy, including exercise, MT, electrotherapy, and combined or multimodal approaches to managing shoulder pain	No report	*N* = 16, 6 of them systematic reviews (100 to 10,000 patients) with moderate and low evidence for MT	A strong recommendation can be made for exercise therapy as the first-line treatment to improve pain, mobility and function in patients with subacromial shoulder pain. Manual therapy may be integrated, with a strong recommendation as additional therapy
Pollack Y et al. [55]	To determine whether manual therapy, consisting of deep massage, myofascial release or joint mobilization is effective in treating plantar heel pain	VAS, PPT, SF-36 questionnaire: Physical function Bodily pain General health General health: Emotional role Vitality	*N* = 6 RCT (177 patients intervention group) Treatment duration: 4 weeks–12 months Outcomes relating to joint mobilizations are controversial	Five studies (from 6) showed a positive short-term effect after MT treatment, mostly soft tissue mobilizations, with or without stretching exercises for patients with plantar heel pain compared to other treatments. MT effectiveness is still under debate
Salamh P et al. [60]	To determine the effectiveness and fidelity of studies using MT techniques in individuals with KOA	VAS, ROM, WOMAC, KOOS, PSFS, quadriceps muscle peak torque, 6 min walk test, KOOS Weeks to 9 months self-reported function	*N* = 12 studies (324 patients); meta-analysis MT techniques individualized based on examination findings	MT appears to be moderately effective for improved self-reported function, specifically as an adjunct to another treatment and versus comparators of no treatment or other treatments; support the clinical utility of MT for knee OA

Table 4 (Continued)

Author	Target/treatment	Assessment	Studies included/comments	Outcome
Tsokanos A et al. [67]	To evaluate the short- and long-term efficacy of MT in knee OA in terms of decreasing pain and improving knee ROM and functionality	VAS, ROM, WOMAC, muscle strength	*N* = 6 RCTs; (40–300 patients) Intervention 2 to 24 weeks Re-evaluation differed	MT can induce a short-term reduction in pain and an increase in knee ROM Regarding the long-term benefits of MT, the research findings were inadequate for making safe and reliable conclusions
Xu Q, Chen B et al. (2017) [74]	To evaluate the effectiveness and adverse events of MT compared to other treatments for relieving pain, stiffness and physical dysfunction in patients with KOA	WOMAC, pain, stiffness, function	*N* = 14 studies (424 patients) Meta-analysis Evidence may be limited by potential bias and poor methodological quality of included studies	The meta-analysis showed favourable effects of MT on pain relief and superior effects on stiffness Preliminary evidence suggests that MT might be effective and safe for improving pain, stiffness and physical function in KOA patients and could be treated as complementary and alternative options (?)

BCTQ Boston Carpal Tunnel Questionnaire, *CMAP* compound muscle action potential, *CTS* carpal tunnel syndrome, *KOA* knee osteoarthritis (OA), *KOOS* Knee Injury and Osteoarthritis Outcome Score, *MT* manual therapy, *NPRS* numeric pain rating scale, *PPT* pain pressure test, *PSFS* patient-specific functional scale, *ROM* range of motion, *SF-36* short form 36, *SM* spinal manipulation, *SMT* spinal manipulative therapy, *WOMAC* Western Ontario and McMaster Universities Osteoarthritis Index, *VAS* visual analogue scale

large and non-quantified variation in the spinal manipulation, and by the unknown heterogeneity of LBP patients [18, 21, 59]. There are a great number of studies which report that the manual techniques are provided by persons skilled and experienced in manual medicine treatment techniques and show a high intra- and interrater reliability, equivalent to high quality in the provided treatment variations.

Again, it should be particularly emphasized that adequate execution of both the examination and the treatment techniques is a combination of haptic and fine motor perception abilities. These skills are only perfected in a motor learning process in practical lifelong everyday activity. There are a large number of factors and variables influencing the success of MM. However, we do not think that this is fundamentally different from the conditions in other clinical disciplines.

Concentrating on the form used to describe treating pain and discomfort in the musculoskeletal system in the different parts of the body, it is noticeable that we not only encounter different treatment techniques but also differently qualified therapists and treatment providers, named as practitioners, doctors, manual medicine specialists, osteopaths, chiropractors and physiotherapists. One reason for this may be that there are different occupational titles and training paths in the single countries. The included studies are mostly in English language, some in Spanish or Portuguese, but the authors are from all over the world. There is also a great variety in the applied techniques described: different forms of MT, SMT, manipulation therapy, manipulation, HVLA, spine thrust, mobilization, hands-on therapy, physical therapy, osteopathic manipulative treatment, etc. With few exceptions, the individual treatment methods are not defined. The biggest shortcoming, however, is the missing description of the treatment carried out, the sequence and duration of treatment, and the procedure of the treatment technique itself. This makes it extremely difficult to compare treatments from different studies and prevents the studies from being repeated by other investigators for verification.

Masic et al. stated in 2008: "Evidence-based medicine (EBM) is the conscientious, explicit, judicious and reasonable use of modern, best evidence in making decisions about the care of individual patients. EBM integrates clinical experience and patient values with the best available research information. … The practice of evidence-based medicine is a process of lifelong, self-directed, problem-based learning in which caring for one's own patients creates the need for clinically important information about diagnosis, prognosis, therapy and other clinical and health care issues. It is not a 'cookbook' with recipes, but its good application brings cost-effective and better health care. The key difference between evidence-based medicine and traditional medicine is not that EBM considers the evidence while the latter does not. Both take evidence into account; however, EBM demands better evidence than has traditionally been used" [44].

In regular meetings of the MM societies, academies, teachers and expert commissions, opinions and convictions from clinical experience are agreed on and published in relevant international journals. This corresponds to level IV of the evidence classes according to the recommendations of the Agency for Healthcare Research and Quality (AHRQ). A higher level of evidence is dependent on methodologically high-quality non-experimental studies such as comparative studies, correlation studies or case–control studies (level III) and on methodologically high-quality non-experimental studies such as comparative studies, correlation studies or case–control studies (level III) and high-quality studies without randomization (level IIb) as well as sufficiently large, methodologically high-quality RCTs (level Ib).

The levels are explained as follows [47]:

– High quality of evidence: further research is unlikely to change our confidence in the estimate of effect. There are consistent findings among 75% of RCTs with a low risk of bias that can be generalized to the population in question. There are sufficient data, with narrow confidence intervals. There are

Table 5 Systematic reviews concerning additional topics

Author	Target/Treatment	Assessment	Studies included/comments	Outcome
Abaraogu et al. [1]	Efficacy of manipulative therapy in women with primary dysmenorrhea	Pain relief (VAS, PPT, pain rating index) Quality of life (menstrual distress questionnaire)	*n* = 4 studies, 3 thereof for meta-analysis Spinal manipulative therapy Bilateral global pelvic manipulation technique Reflexology	Moderate methodological quality Significant evidence of pain reduction → manipulative therapy as adjunct therapy Lack of blinding and outcome concerning quality of life
Arumugam et al. [4]	Effects of external pelvic compression (EPC) on form closure, force closure and neuromotor control of the lumbopelvic spine	Doppler imaging of vibrations Radiographic lumbopelvic angles and erector spinae muscle activity in standing, erect and slump sitting Active straight leg raise test EMG activity of abdominal and thoracic muscles Ultrasonography of pelvic floor movement Pain scale (VAS) Isometric measures, MVC	*n* = 18 studies 15 used a pelvic compression belt 2 used manual compression 1 used mechanical compression with device	Moderate evidence for EPC in decreasing laxity of SIJ, changing lumbopelvic kinematics, altering selective recruitment of stabilizing musculature and reducing pain Limited evidence for EPC on decreasing sacral mobility and affecting strength of muscles surrounding the SIJ Results might not necessarily apply to sustained application of EPC
Chow et al. [8]	Assessment of studies evaluating spinal manipulative therapy (SMT) and infectious disease and immune system outcomes	Level of selected immunological biomarkers	*n* = 13 studies, 6 thereof RCTs	No clinical studies to support or refute the efficacy or effectiveness of SMT in preventing the development of infectious disease or improving disease-specific outcomes Preliminary data that SMT has short-term changes in selected immunological and endocrine biomarkers among asymptomatic participants
Chung et al. [9]	The association between cervical spine manipulation and internal carotid artery (ICA) dissection—safety of cervical spine manipulation	n.a.	No studies were found measuring the incidence or association of cervical spine manipulation and ICA dissection	Incidence of ICA dissection and cervical manipulation is unknown Besides some case reports, there is no epidemiologic evidence for association to validate this hypothesis
Coté et al. [10]	The global summit on the efficacy and effectiveness of spinal manipulative therapy for the prevention and treatment of non-musculoskeletal disorders	Asthma: peak expiratory flow Infantile colic: parents-perceived global improvement Hypertension: blood pressure, heart rate Dysmenorrhea: pain (VAS) Migraine: migraine days per month	*n* = 6 studies RCTs, all suitable for meta-analysis	Acceptable or high methodological quality SMT for management of infantile colic, childhood asthma, hypertension, primary dysmenorrhea, and migraine—not preventing the occurrence of non-musculoskeletal disorders RCTs with high of acceptable quality
Da Silva et al. [13]	Manual therapy as treatment for chronic musculoskeletal pain in female breast cancer survivors	Pain (VAS), PPT (algometer) Shoulder ROM SF-36/DASH Breast cancer-specific quality of life Arm/breast symptoms Pain catastrophizing (PRSS)	*n* = 5 studies RCTs, all suitable for meta-analysis Myofascial induction/release/therapy Classic massage Ischemic compression of trigger points	Positive effect on upper limbs and thorax of female breast cancer survivors Manual therapy decreased chronic musculoskeletal pain intensity and increased pain pressure threshold No difference in quality of life 3 studies of good quality

Table 5 (Continued)

Author	Target/Treatment	Assessment	Studies included/comments	Outcome
Fernández-López et al. [17]	Effects of manual therapy on the diaphragm in the musculoskeletal system	Ultrasonographic diaphragm mobility Spinal motion (cervical and lumbar ROM) Posterior chain mobility/flexibility: finger-to-floor test/hamstrings flexibility/sit-and-reach test/Schober-test Pain: VAS, PPT (C4 level) Abdominal and rib cage excursion (Th4-Level) Assessment pain and function/questionnaires	*n* = 9 studies (no meta-analysis) Focus on diaphragm muscle Stretching or myofascial release Lumbar manual techniques	Manual therapy to diaphragm is effective: immediate increase in diaphragmatic mobility and thoracoabdominal expansion Improvement in posterior muscle chain flexibility Improvement in lumbar and cervical ROM No long-term studies No symptomatic population Neurophysiologic mechanism is unknown 8 × high or very high quality, deficits in blinding
Kamonseki et al. [31]	Effects of manual therapy on fear avoidance, kinesiophobia and pain catastrophizing in individuals with chronic musculoskeletal pain	Fear avoidance beliefs questionnaire Tampa scale of kinesiophobia Pain catastrophizing scale	*n* = 11 studies, all suitable for meta-analysis (1 not-RCT) Joint mobilization Soft tissue techniques/mobilization Myofascial release Longitudinal sliding Deep pressure massage (ischemic compression Massage Muscle energy Hold–relax techniques Functional techniques	Manual therapy not significantly different to no treatment/other treatment in reducing fear-avoidance, kinesiophobia or pain catastrophizing Low or very low level of evidence Small to moderate effect size, but not significantly different to no or other treatment
Kendall et al. [32]	Effects of manual therapies on stability in people with musculoskeletal pain	Balance measures: Gait speed Timed up-and-go test (TUG) Step test Sit-to-stand test Balance Performance: Static balance Modified Schober's test Force plate centre of pressure Postural stability Romberg's test No measuring of falls	*n* = 26 studies (mostly lower limb osteoarthritis or low back pain), 8 studies thereof for meta-analysis	Significant improvement of gait speed and TUG Only short-term (not in the long-term follow-up) No clear association between pain reduction and measures of stability Except of performance bias, risk of bias was generally low or of unclear level
Kovanur-Sampath et al. [35]	Changes in biochemical markers following spinal manipulation	Biochemical markers: neuropeptides, inflammatory and endocrine biomarkers from blood, urine or saliva Immediate (up to 30 min) and short-term (hours after intervention)	*n* = 8 studies (randomized controlled trials and clinical trials) Spinal manipulation as intervention (healthy and painful)	Moderate-quality evidence on influence on biochemical markers Moderate-quality evidence: significant difference in favour of spinal manipulation (cortisol level) Low-quality evidence: increasing substance-P, neurotensin and oxytocin level; no influence on epinephrine or nor-epinephrine level Modulation of pain and inflammation possible No statement on clinical importance of change in biochemical markers
Navarro-Santano et al. [49]	Effects of joint mobilization on clinical manifestations of sympathetic nervous system activity	Skin conductance Skin temperature	*n* = 18 studies, 17 thereof for meta-analysis Mobilization (cervical, thoracic, lumbar and upper limbs region) 7 RCT's 14 of 18 studies on asymptomatic healthy subjects	Significant increase of skin conductance and a decrease in temperature after mobilization Risk of bias was generally low Moderate evidence on a sympathoexcitatory effect of joint mobilization Level of evidence downgraded by heterogenicity

Table 5 (Continued)

Author	Target/Treatment	Assessment	Studies included/comments	Outcome
Rechberger et al. [57]	Effectiveness of an osteopathic treatment on the autonomic nervous system (ANS)	Cardiovascular: heart frequency, heart rate volume Sympathetic activity: cortisol level Pain intensity Skin conductance/ temperature Upright stance stability	*n* = 23 studies 10 RCT's, 1 clinical multicentre study, 1 CCT, 5 randomized cross-over studies, 5 randomized pilot studies, 1 single case study	Good level of evidence: 3 as high, 11 as moderate, 8 as low Methodological quality is moderate Significant change of ANS by HVLA Significant change in the treatment of suboccipital region There might be "responder" and non "non-responder" *No statement* – concerning cranial osteopathic techniques due to lack of quality; – concerning effectiveness of mobilization cervical and thoracic due to low evidence; – concerning whether change in ANS took place in the sympathetic or parasympathetic system
Roura et al. [58]	Do manual therapies have a specific autonomic effect?	Autonomic markers (examples): Skin conductance Skin temperature Heart rate variability Heart rate Blood pressure Microneurography Spillover Pupil light reflexes Electrodermal activity Thermal infrared imaging Skin blood flow	*n* = 12 reviews, all included RCT's, partly other study-designs Spinal mobilization (1 × cervical) Spinal manipulations Cranial techniques Myofascial techniques Peripheral mobilization	5 rated as low risk of bias Manual therapies can have an effect on both sympathetic and parasympathetic system Inconsistent results due to differences in the methodology No discrimination depending on the body region Skin conductance demonstrated a consistent acute sympaticoexcitatory effect for spinal mobilizations Cardiovascular parasympathetic system activation seems to be elicited by manipulations to the upper neck and lumbar spine and by myofascial techniques *Clinical relevance unclear:* – Mostly healthy subjects – Only short-term effects – Very few correlations with patient-related-outcome-measures
Schulze et al. [62]	Efficacy of manual therapy for pain, impact of disease and quality of life in the treatment of fibromyalgia	Pain (VAS) Disease impact (Fibromyalgia Impact Questionnaire, SF-36)	*n* = 7 studies, 4 thereof for meta-analysis Myofascial mobilization/ release	Low to moderate evidence Heterogeneity of the included studies Only short-term results Myofascial release (IG) vs. lymphatic drainage (CG): higher pain intensity and FM impact for IG Myofascial release (IG) vs. sham magnetotherapy (CG): improvement in different quality of life subscales and pain intensity for IG Myofascial release (IG) vs. pilates (CG): higher pain intensity and FM impact for IG General osteopathic treatment (IG) vs. control (CG): reduced pain intensity and reduction in the impact of FM (slow mobilization of soft and articular tissues through wide, smooth, rhythmic, continuous movements)
Slater et al. [63]	The effectiveness of subgroup-specific manual therapy for low back pain	Pain (VAS, NRS) Activity (Oswestry Low Back Pain Disability Questionnaire)	*n* = 7 studies 3 subgroups: Centralization of symptoms (CoS) with repeated lumbar extension CoS as well as symptom reproduction in three out of four provocative tests for SIJ pain A predetermined clinical prediction rule for spinal manipulation	Significant treatment effects found for pain and activity at short- and intermediate follow-up in favour if manual therapy (subgroup specific) Low quality

Table 5 (Continued)

Author	Target/Treatment	Assessment	Studies included/comments	Outcome
Tramontano et al. [66]	Vertigo and balance disorders—the role of osteopathic manipulative treatment	e.g. dizziness handicap inventory (DHI) Stabilometric assessment Mini-BEST test Sensory organization test (SOT)	*n* = 5 studies Osteopathic manipulative treatment (soft tissue, articulatory and muscle energy techniques, myofascial release, HVLA to thoracic/lumbar spine, counterstrain, balanced ligamentous technique)	(Weak) positive outcome on balance disorders through different outcomes Encouraging the connection of conventional medicine and evidence-based complementary medicine Studies of higher evidence are required, limited generalizability
Ughreja et al. [68]	Effectiveness of myofascial release on pain, sleep and quality of life in patients with fibromyalgia syndrome	Pain (VAS, McGill Pain Questionnaire, Nordic musculoskeletal questionnaire)/pressure pain threshold) Sleep (Pittsburgh sleep quality index) Quality of life (fibromyalgia impact questionnaire, SF-36) Anxiety Depression Tender points Fatigue Postural stability Clinical global impression severity Range of motion Sit-to-reach-test	*n* = 6 studies, two thereof for meta-analysis on pain 4 to 40 sessions and 50 to 90 min (myofascial release)	Large significant effect on pain post-treatment and moderate effect at 6 months post-treatment Compared to sham and no therapy Moderate evidence Studies of higher evidence are required
Webb et al. [70]	Myofascial techniques—effects on joint range of motion (ROM) and pain	Joint range of motion (active mouth opening, interincisal opening, cervical ROM, tape measurement, digital inclinometer, goniometer) Pain (VAS, PPT)	*n* = 9 studies, 2 thereof for meta-analysis Randomized controlled trials Muscle energy technique Strain counterstrain Ischaemic compression Myofascial release Neuromuscular technique Positional release	Every single trial concluded the positive effect of myofascial techniques on range of motion and pain Moderate effect size for jaw opening with latent trigger points in masseter muscle High levels of data heterogeneity within the other trials Lack of power calculation, bias prevention, validated outcome measures, reporting between-group differences, effect sizes and confidence intervals
Wong et al. [73]	Strain counterstrain (SCS) technique to decrease tender point palpation pain compared to control conditions	Palpation pain on visual analogue scale (VAS) or numeric rating scale (NRS)	*n* = 5 studies, 2 thereof for meta-analysis Randomized controlled trials with isolated SCS treatment 8 or more of the 12 methodological criteria were fulfilled	Pooled: significant reduction of tender point palpation pain Low evidence quality No statement on long-term pain, impairment or dysfunction

VAS visual analogue scale, *NRS* numeric rating scale, *PPT* pain pressure threshold, *SF-36* Short-Form-36

no known or suspected reporting biases. (All of the domains are met).
- Moderate quality of evidence: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. (One of the domains is not met).
- Low quality of evidence: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. (Two of the domains are not met).
- Very low quality of evidence: we are very uncertain about the estimate. (Three of the domains are not met).

Prerequisites for evidence-based diagnostics in MM are good reproducibility, validity, sensitivity and specificity studies of the diagnostic procedures. To ensure the quality of such studies, the International Academy for Manual Musculoskeletal Medicine has developed a "reproducibility protocol for diagnostic procedures in MM" in recent years. "The protocol can be used as a kind of 'cook book format' to perform reproducibility studies with kappa statistics. It makes it feasible to perform reproducibility studies in MM clinics and by educational boards of the MM societies" [53].

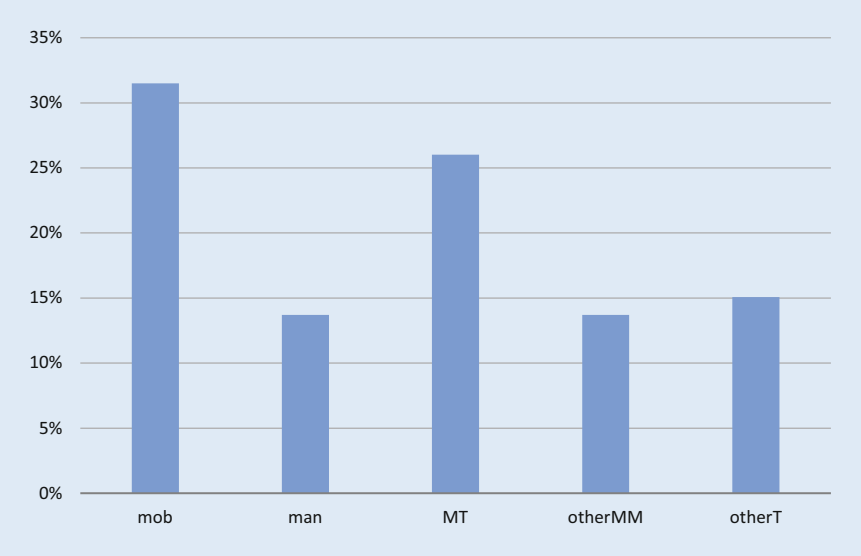

Fig. 2 ▲ Distribution of keywords (*mob* mobilization, *man* manipulation, *MT* manual therapy, *otherMM* other manual medicine treatment, *otherT* other treatment)

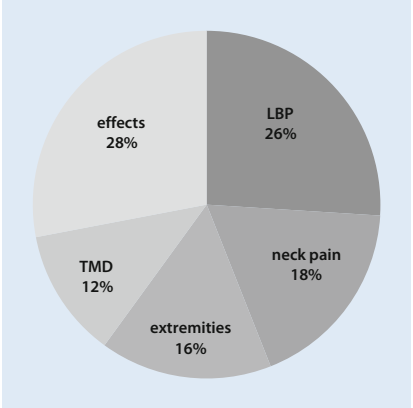

Fig. 3 ▲ Distribution of study questions. *LBP* lower back pain, *TMD* temporomandibular disorder

Conclusion

Based on the available scientific material, it can be concluded that a general EBM level III is available, with individual studies reaching level II or Ib, which creates the prerequisite and the ability to perform tasks to a satisfactory or expected verification (validity) of MM diagnostic and therapeutic techniques.

The results of this systematic review show that

- Spinal manipulation and mobilization and MT were significantly more efficacious for neck/low back pain than no treatment, placebo, physical therapy or usual care in reducing pain.
- SMT is a cost-effective treatment to manage spinal pain when used alone or in combination with general practitioner (GP) care or advice and exercise compared to GP care alone, exercise or any combination of these.
- SMT has a statistically significant association with improvements in function and pain improvement in patients with acute low back pain.
- Preliminary evidence that subgroup-specific manual therapy may produce a greater reduction in pain and increase in activity in people with LBP when compared with other treatments. Individual trials with a low risk of bias found large and significant effect sizes in favour of specific manual therapy.
- Upper cervical manipulation or mobilization and protocols of mixed manual therapy techniques presented the strongest evidence for symptom control and improvement of maximum mouth opening.
- Musculoskeletal manipulation approaches are effective for the treatment of temporomandibular joint disorders—here is a larger effect for musculoskeletal manual approaches/manipulations compared to other conservative treatments for temporomandibular joint disorder.
- MM is helpful and facilitating in the management of several diseases, with an influence on range of motion, pain intensity, flexibility and parts of the autonomic nervous system.

The results of the available reviews and the evidence found on the effect of manual medicine treatment with the view to inclusion of manual therapy in guidelines are regarding treatment of acute and chronic pain due to the musculoskeletal system, especially including spine, joints and muscles.

All reviews mentioned call for further qualitative studies in order to consolidate and increase the level of evidence.

The previous initial shortcomings of the studies must be overcome:

- Clear elaboration of questions.
- Exact description of manual medicine practice/manual techniques.
- Lowering the bias in patient inclusion.

The EBM-oriented physicians and therapists of tomorrow's manual medicine treatment have three tasks [44]:

- To use evidence summaries in clinical practice.
- To help develop and update selected systematic reviews or evidence-based guidelines in their area of expertise.
- To enrol patients in studies of treatment, diagnosis and prognosis on which medical practice is based.

The topicality of this statement has not changed to this day.

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Declarations

Conflict of interest. L. Beyer, S. Vinzelberg, and D. Loudovici-Krug declare that they have no competing interests.

For this article, no studies with human participants or animals were performed by any of the authors. All studies mentioned were in accordance with the ethical standards indicated in each case.

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Zusammenfassung

Evidenz (-basierte Medizin) in der manuellen Medizin/manuellen Therapie – zusammenfassende Übersicht

Ziel: Ziel der vorliegenden Übersichtsarbeit war eine Auswertung des aktuellen Erkenntnisstands in der manuellen Medizin bzw. in der manuellen Therapie.
Methoden: Bei der Literatursuche lag der Fokus auf systematischen Übersichten, begrenzt auf die Sprachen Englisch oder Deutsch, die bis Anfang 2022 in der Datenbank PubMed vorhanden waren und sich auf die Behandlung mittels manueller Medizin bezogen. Die Suche umfasste die Begriffe (1) „manipulation", (2) „mobilization", (3) „functional/musculoskeletal" und (4) „fascia". Die Checkliste für systematische Übersichten gemäß Critical Appraisal Skills Programme (CASP) wurde verwendet, um die einbezogenen Übersichtsarbeiten auf eine übersichtliche Weise zu präsentieren.
Ergebnisse: In die Auswertung wurden 67 Publikationen eingeschlossen, die in 5 Kategorien unterteilt waren: Schmerzen des unteren Rückens, Nackenschmerzen, Extremitäten, temporomandibuläre Störungen und sonstige Auswirkungen. Die Ergebnisse wurden in Übereinstimmung mit den Fragestellungen der Studie gruppiert.
Schlussfolgerung: Auf der Grundlage aktueller systematischer Übersichtsarbeiten liegt eine allgemeine Evidenz der Stufe III vor, dabei erreichten einzelne Studien sogar Stufe II oder Ib. Diese Ausgangssituation ermöglicht eine valide Behandlung mit manueller Medizin oder manueller Therapie.

Schlüsselwörter
Schmerzen des unteren Rückens · Temporomandibuläre Störung · Nackenschmerzen · Extremitäten · Muskuloskelettal

Speksnijder CM (2020) Effects of physical therapy for temporomandibular disorders on headache pain intensity: a systematic review. Musculoskelet Sci Pract 50:102277
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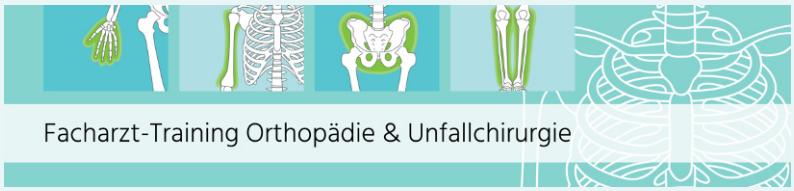

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