

Therapy for Musculoskeletal Pain

Dominic Müller^{1*}, Barbara Keller¹, Asha-Naima Ferrante^{1,2}, Caroline Rimensberger¹, Maurizio Alen Trippolini^{3,4,5†}, Maria M Wertli^{1†}

¹Department of General Internal Medicine, University Hospital of Bern, Inselspital, Bern, Switzerland

²Department of Psychology, University of Bern, Bern, Switzerland

³Bern University of Applied Sciences, Department of Health, University Hospital Bern, Inselspital, Bern, Switzerland

⁴Institute of Physiotherapy, University Hospital of Bern, Inselspital, Bern, Switzerland

⁵Massachusetts General Hospital (MGH) Institute of Health Professions, Charlestown, Boston, MA, United States

[†]These authors contributed equally to this work.

**Corresponding author:* Dominic Müller, dominic.mueller1@students.unibe.ch

Copyright: © 2023 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: Acute musculoskeletal pain is common and often heals spontaneously. In contrast, chronic musculoskeletal pain is one of the leading causes of pain-related disability. The current recommendations for the assessment and treatment of musculoskeletal pain are discussed in this paper.

Keywords: Musculoskeletal pain; Acute pain; Chronic pain; Pharmacological; Non-pharmacological

Online publication: June 26, 2023

1. Introduction

Globally, 20%–33% of the population is affected by musculoskeletal pain ^[1]. Musculoskeletal pain develops from injuries to bones, muscles, tendons, ligaments, or nerves ^[2]. Chronic musculoskeletal pain is among the 10 most common causes of pain-related functional limitations ^[1]. Neck pain and back pain are among the most common causes. In the Swiss Health Survey, almost half of the respondents suffer from back or low back pain, and about one third suffer from shoulder, neck, or arm pain ^[3]. Lumbar back pain alone accounts for about 6% of the total healthcare cost in Switzerland ^[4]. Acute pain is a warning indicator aimed at preventing further injuries ^[5]. However, the individual perception of pain is influenced by various factors, such as nociception, inflammatory processes, nerve injuries, and pre-existing sensitization ^[6].

If pain persists longer than expected for the recovery of an injury (usually 3 months), it is referred to as chronic pain ^[7]. In the updated ICD-11 classification, chronic primary pain is classified as a separate diagnosis, underpinning its importance ^[7]. The goal of treatment is to avoid overtreatment and prevent chronification of the pain through timely and effective treatment. In this context, it is important to avoid the diagnostic and treatment pitfalls in acute pain (**Table 1** ^[8]). In addition, in patients with pain that persists longer or is more severe than expected, evidence of biopsychosocial factors should be sought.

2. Acute pain assessment

The assessment of musculoskeletal pain is primarily based on a detailed medical history and physical examination with assessment of mobility, muscle strength, and neurological function ^[8]. Numerous studies

have shown that contextual factors (*e.g.*, professional appearance, gestures, physician’s touch, and equipment) surrounding the examination and treatment have a significant influence on the perception of pain [9]. Guidelines have primarily advised against imaging diagnostics in the absence of red flags [10-12]. In a study of acute lumbar back pain, early magnetic resonance imaging (MRI) did not improve clinical outcomes, and patients with knowledge of their MRI findings had a lower quality of life than those who did not know their imaging findings [13]. Imaging findings that are not directly related to the cause of pain also carry the risk of overtreatment [8]. Therefore, the indication for imaging should be specific, and the decision for imaging should only be made when it significantly influences the treatment [11]. Other indications include the progression of symptoms or an inadequate response to effective and correctly administered treatment [8,11].

Table 1. Diagnostic and treatment pitfalls in musculoskeletal pain

<p>(1) Overuse of imaging: Although many musculoskeletal pains do not have alarming signs or evidence of a specific cause, imaging is often used, with possible consequences, including overtreatment of incidental findings and unnecessary interventions.</p> <p>(2) Overuse of surgery: Knee arthroscopy for knee osteoarthritis, subacromial decompression, and rotator cuff repair of the shoulder are increasingly common. However, high-quality studies have failed to provide evidence that these procedures are more effective than non-surgical procedures.</p> <p>(3) Overuse of opioids: Although randomized trials have not shown that opioids have better efficacy for acute and chronic musculoskeletal pain, they are increasingly prescribed.</p> <p>(4) Failure to provide education and counselling: Education and counselling about the cause, prognosis, and treatment are the cornerstones of musculoskeletal pain management. However, this is only done in a minority of patients with lumbar back pain.</p> <p>(5) Lack of exchange between multimodal practitioners: In view of the different causes of musculoskeletal pain, several specialties are often involved. A lack of exchange can lead to overdiagnosis, overtreatment, and uncertainty on the part of the patient, ultimately contributing to the chronification of pain.</p>

The importance of communication with patients in the acute phase of pain is underestimated. Communication influences patients’ expectations and behavior (*e.g.*, compliance to treatment) and thus the course of the disease [14]. It is common for patients to want to know the exact cause of their pain. Through imaging, patients (and physicians) hope to gain a better understanding of the disease, with the consequence of imaging overuse and potentially negative consequences. In order to respond effectively to expectations and fears, both affective (building therapeutic relationship and emotional rapport) and cognitive communication (conveying and imparting knowledge, explaining the prognosis, ruling out serious pathologies, and discussing the treatment plan) are important [15]. The motivational interviewing approach in which listening, questioning, and informing are balanced can trigger behavioral change in patients with acute and chronic pain and motivate them [16,17]. Ideally, the aim is for the patients themselves to present arguments in favor of a change in behavior [18].

3. Assessment of the transition from acute to chronic pain

Figure 1 illustrates the currently recommended managed-care model for pain. Measures should be adapted depending on the intensity and duration of pain. Several factors can increase the risk of a chronic course. These include biological factors (central or peripheral sensitivity), the placebo effect, and psychosocial factors. It is important that these influencing factors are recognized and addressed early on in order to prevent the chronicity of pain.

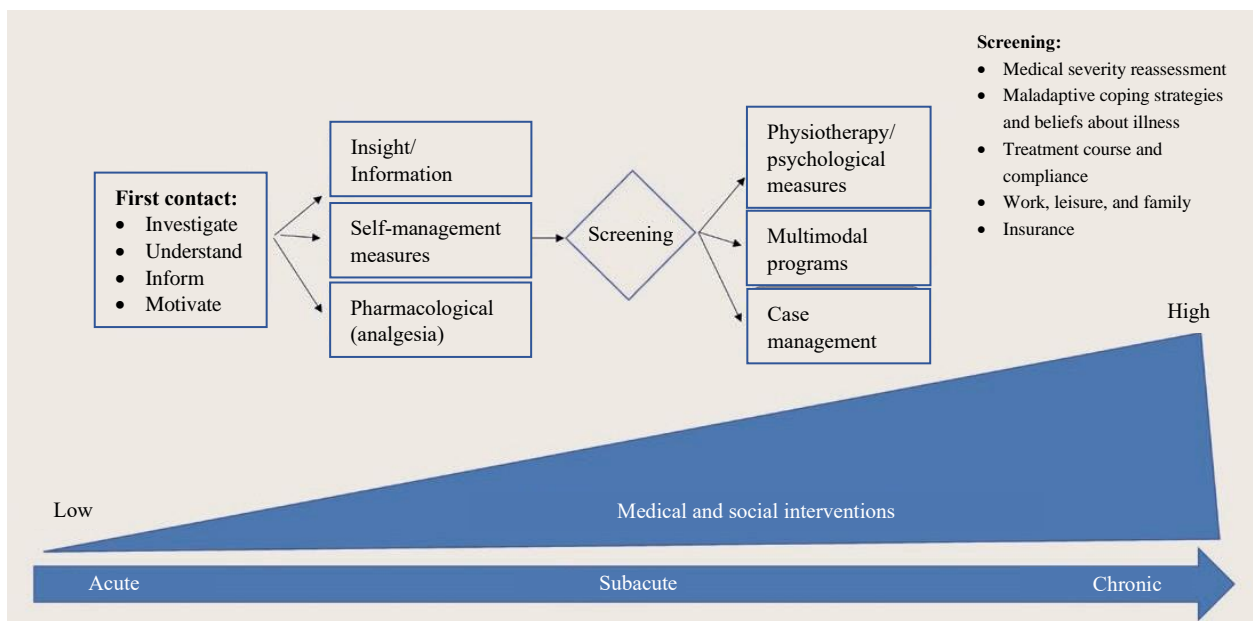


Figure 1. Managed-care model for musculoskeletal pain

Sensitization occurs through previous pain experiences, which can lead to lowered excitation threshold (peripheral sensitization) or increased excitability to less stimuli in the central nervous system (central sensitization) ^[19]. In the case of sensitization, there is decoupling of the perception of pain from the actual stimulus, which can influence the handling of pain (*e.g.*, hyperalgesia and allodynia) ^[20-22]. In contrast to the placebo effect, the expectation of a negative consequence brings about actual symptoms (nocebo effect), without a connection between the agent and the symptoms. Nocebo reactions can be triggered by unintentional negative suggestions on the part of physicians and nurses ^[23]. Psychological, social, and occupational factors also influence the handling of pain. They are referred to as yellow, blue, or black flags in English-language literature (**Table 2**) and may contribute to the chronification of pain ^[24]. Sample questions used to assess the risk factors are shown in **Table 2** ^[25].

Table 2. Factors influencing pain

Warning signs	Factors and sample questions
Red flags	Warning signs for a serious illness that requires further clarification
Yellow flags	Indications of psychosocial factors that may have unfavorable influence on the way pain is dealt with: <ol style="list-style-type: none"> (1) Catastrophizing: What does an increase in pain mean to you? (2) Avoidance behavior: Do you avoid movements/actions out of fear of pain? (3) Fear: Are you worried that you will have pain again? (4) Depressive feelings: How do you feel? (5) Anger/frustration: Why do you think you have this pain? How do you deal with it? (6) Pain beliefs: How long do you think your pain will last? (7) Self-efficacy: What do you do concretely to deal with the pain/discomfort? What do you do to alleviate the pain/discomfort?
Blue flags	Socio-economic factors: Job satisfaction, working conditions, and social factors <ol style="list-style-type: none"> (1) Do you think your pain is caused/worsened by work? (2) Are you worried about resuming certain activities? (3) Do you think that your work could be temporarily modified?
Black flags	Unemployment, insurance factors, family support, legal processes

Validated questionnaires, such as STarT MSK screening tool [26], can be adapted to customize measures. Clinical examination provides additional indications of pain avoidance behavior or maladaptive loading [27]. If modifiable factors are taken into account in the treatment, the development of chronic pain can be prevented. The development of an individualized biopsychosocial disease model and a “both/and” attitude, as opposed to an “either/or” approach, offers the opportunity to destigmatize psychosocial factors in the etiology, intensity, and maintenance of pain. To this end, a basic empathic and coping-oriented attitude is of central importance to building a sustainable working relationship based on partnership [28]. **Table S1** in **Appendix** lists 14 key treatment principles for musculoskeletal pain, as recommended by high-quality guidelines [8].

4. Non-pharmacological treatments for acute musculoskeletal pain

In the case of acute musculoskeletal pain without warning signs, non-pharmacological and, if necessary, pharmacological measures should be used simultaneously. In this context, non-pharmacological measures are often equally or even more effective than analgesics and have been used since ancient times. Individual pain processing depends on genetic factors, psychological state, neurophysiology, general health, and comorbidities. Therefore, non-pharmacological measures should be individualized in the acute phase and continuously adjusted in consultation with the patient in order to achieve an effect.

Although the effectiveness of non-pharmacological measures has been questioned [29], the pain-relief measures often performed in the first few days following musculoskeletal injury are known by the acronym RICE (Rest, Ice, Compression, and Elevation). Especially for nonspecific back pain, it is critical that patients remain active. Immobilization and prolonged rest should be avoided, and patients should be informed of the extent to which they can be physically active and which self-management measures can reduce the pain. Massaging and mobilizing the joints can activate inhibitory receptors (serotonin, norepinephrine, adenosine, and cannabinoids) and thus produce an analgesic effect [30]. Additional analgesics may be necessary for patients to remain active.

Transcutaneous electrical stimulation (TENS) and other local treatments (laser, ultrasound, acupuncture, and superficial heat and cold applications) only have little and short-term effects on pain reduction [31]. Only recently have the mechanisms of pain modulation by TENS been understood. Most reviews (small, heterogeneous studies) have shown that TENS and manual manipulation for acute low back pain can briefly reduce pain and improve daily function [32]. The most common side effects after manual manipulation are short-term increase in pain, muscle stiffness, and headache (in 50%–65% of patients).

5. Non-pharmacological treatments for chronic musculoskeletal pain

Stratified treatment programs (**Figure 1**), which allow more targeted interventions by examining individual risk factors, are the way forward [33]. If these programs are combined with case management and embedded in an onboarding process with employers, a reduction in pain and functional limitations can be achieved with lower costs [34,35]. In primary care, however, there are many barriers to the implementation of evidence-based treatment recommendations [36]. Named are the high expectations of patients for physicians to initiate medication or perform imaging, the disinterest and lack of time to address risk factors, and the lack of knowledge or availability of nonsurgical treatment options [37]. In Switzerland, outpatient multimodality programs are poorly established, and there are uncertainties around funding [38]. Structured care pathways are recommended with the aim of reducing overuse [39].

The best studied treatments are active training interventions. Regular physical training, as evidenced in both animal models and in humans, leads to exercise-induced analgesia through the activation of central inhibitory systems with an increase in serotonin levels and the release of endogenous opioids [40]. The effect is evident during strength and endurance training. However, the analgesic effect occurs only after a certain

regularity of active training ^[41]. This explains why patients with chronic musculoskeletal pain would complain of exaggerated pain at the start of any exercise ^[40]. In a recent Cochrane review, exercise-oriented interventions for chronic back pain were more effective in reducing pain and improving function than placebo interventions (249 trials, with 24,486 patients; moderate evidence) ^[42]. In a network meta-analysis, exercise-oriented interventions such as Pilates, McKenzie, and exercise-oriented rehabilitation (functional restoration programs) were significantly more effective in reducing pain and the restriction in daily activities than other measures (education, manual therapy, back school, electrical/psychotherapy, anti-inflammatory drugs, and relaxation) ^[43]. Stretching, trunk strengthening, endurance training, and yoga also showed some effects.

Mind-body therapies (*e.g.*, meditation and relaxation techniques, hypnosis, and behavioral therapy) are becoming increasingly popular. In a review of small, randomized trials, these therapies showed some reduction in pain and slight reduction in opioid use ^[44]. However, these findings must be validated by larger trials. The results of learning self-management measures via group classes were disappointing, as the effects on pain and functional limitations were insignificant, without improvement in coping behaviors ^[45].

In order to address the complex psychosocial aspects of chronic musculoskeletal pain, both inpatient and outpatient multimodal programs are recommended ^[10]. These programs usually include several medical disciplines, physical and psychological, and/or workplace-oriented or social measures. For subacute chronic back pain, multimodal programs are preferred over other interventions (surgical or purely exercise-oriented interventions and general care) to reduce pain, functional limitations, and work disability ^[46,47]. However, it is important to note that women were predominantly included in these multimodal studies, thereby limiting generalizability ^[47]. In addition, multimodal programs for chronic pain were hardly effective for patients with a migration background ^[48].

6. Pharmacological treatment

Good analgesia allows patients to remain active and participate in active therapy. **Table S2** in **Appendix** lists the most important pharmacologic options as well as the most common contraindications and side effects. As first-line therapy, topical and/or oral nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended in the absence of contraindications ^[49]. Paracetamol is no longer ^[12] recommended or only recommended for short use in combination with other drugs ^[31, 49-51]. In a high-quality study ^[31], no clinical effect was observed with its use, and its side effects (especially hepatotoxicity) were nevertheless common. Metamizole, on the other hand, is increasingly being used in Switzerland ^[52], although there have been no studies on its efficacy in musculoskeletal pain. Metamizole is likely to be as effective as NSAIDs but more tolerable ^[53]. The reason for the widespread reluctance of metamizole use is the rare but serious side effect of agranulocytosis. This occurs in approximately 0.5–1.5 cases per million people daily applications ^[53].

For severe pain, weak opioids (tramadol, codeine, and tapentadol) or strong short-acting opioids (if intolerant of weak opioids or with inadequate pain control) should be used cautiously and for as short a time as possible ^[54]. Strong short-acting opioids should be prescribed at the lowest effective dose. The dosage and indication of these opioids should be constantly reviewed ^[54]. A growing number of studies have shown that for acute musculoskeletal pain, strong opioids are not superior to NSAIDs but have significantly more side effects ^[50,55]. In cases of persistent opioid use, the proportion of individuals with withdrawal symptoms upon reduction and the risk of dependence have shown to increase ^[56,57]. The chronic use of opioids for chronic pain can worsen the quality of life ^[58,59], without even improving function or pain control ^[58]. In a randomized trial of patients with chronic musculoskeletal pain, those who received opioids experienced more pain and side effects after 12 months than those who did not ^[58]. Furthermore, the discontinuation of long-term opioid use often leads to improvement in pain intensity, function, and quality of life ^[60].

Intra-articular injections of corticosteroids can provide short-term relief of moderate to severe pain, especially in osteoarthritis-related shoulder and knee pain [31,51]. In the case of nonspecific neck or back pain, such injections are not recommended [31].

There are hardly any studies on the use of cannabis for chronic musculoskeletal pain. According to a systematic literature review, the synthetic cannabinoid nabilone is no more effective than placebos for chronic low back pain due to fibromyalgia, degenerative pain, and/or rheumatoid arthritis [61]. In addition, side effects such as drowsiness, dry mouth, euphoria, ataxia, and headache are expected. Hence, the use of cannabis for musculoskeletal pain is not recommended for the time being [61]. Similarly, the use of benzodiazepines and gabapentinoids for musculoskeletal pain has not received much attention. Their effects are likely insignificant with increased risk of side effects (dizziness, fatigue, difficulty thinking, and visual disturbances) [62,63].

7. Conclusion

In musculoskeletal pain, medical and non-medical factors play an important role in influencing the prognosis. These factors should be considered in the stratified assessment. Communication also plays an important role in the management of musculoskeletal pain, with non-pharmacological measures being the foreground.

Disclosure statement

The authors declare that they have no financial or personal affiliations in connection with this paper.

References

- [1] GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018, Global, Regional, and National Incidence, Prevalence, and Years Lived with Disability for 354 Diseases and Injuries for 195 Countries and Territories, 1990–2017: A Systematic Analysis for the Global Burden of Disease Study 2017. *Lancet*, 392(10159): 1789–1858.
- [2] Gerstman B, Chou K, Burke L, 2021, Musculoskeletal Pain, in *Pain Care Essentials and Innovations*, Elsevier, 73–89.
- [3] Storni M, Lieberherr R, Kaeser M, (eds) 2018, Schweizerische Gesundheitsbefragung 2017 [Swiss Health Survey 2017], Federal Statistical Office (BFS).
- [4] Wieser S, Horisberger B, Schmidhauser S, et al., 2011, Cost of Low Back Pain in Switzerland in 2005. *Eur J Health Econ*, 12(5): 455–467.
- [5] Grichnik KP, Ferrante FM, 1991, The Difference Between Acute and Chronic Pain. *Mt Sinai J Med*, 58(3): 217–220.
- [6] Richebé P, Capdevila X, Rivat C, 2018, Persistent Postsurgical Pain: Pathophysiology and Preventative Pharmacologic Considerations. *Anesthesiology*, 129(3): 590–607.
- [7] Treede RD, Rief W, Barke A, et al., 2019, Chronic Pain as a Symptom or a Disease: The IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). *Pain*, 160(1): 19–27.
- [8] Lin I, Wiles L, Waller R, et al., 2020, What Does Best Practice Care for Musculoskeletal Pain Look Like? Eleven Consistent Recommendations from High-Quality Clinical Practice Guidelines: Systematic Review. *Br J Sports Med*, 54(2): 79–86.
- [9] Rossetini G, Carlino E, Testa M, 2018, Clinical Relevance of Contextual Factors as Triggers of

- Placebo and Nocebo Effects in Musculoskeletal Pain. *BMC Musculoskelet Disord*, 19(1): 27.
- [10] Foster NE, Anema JR, Cherkin D, et al., 2018, Prevention and Treatment of Low Back Pain: Evidence, Challenges, and Promising Directions. *Lancet*, 391(10137): 2368–2383.
- [11] Cuff A, Parton S, Tyer R, 2018, Guidelines for the Use of Diagnostic Imaging in Musculoskeletal Pain Conditions Affecting the Lower Back, Knee and Shoulder: A Scoping Review. *Musculoskeletal Care*, 18(4): 546–554.
- [12] Oliveira CB, Maher CG, Pinto RZ, et al., 2018, Clinical Practice Guidelines for the Management of Non-Specific Low Back Pain in Primary Care: An Updated Overview. *Eur Spine J*, 27(11): 2791–2803.
- [13] Ash LM, Modic MT, Obuchowski NA, et al., 2008, Effects of Diagnostic Information, Per Se, on Patient Outcomes in Acute Radiculopathy and Low Back Pain. *AJNR Am J Neuroradiol*, 29(6): 1098–1103.
- [14] Phillips LA, Leventhal H, Leventhal EA, 2012, Physicians’ Communication of the Common-Sense Self-Regulation Model Results in Greater Reported Adherence Than Physicians’ Use of Interpersonal Skills. *Br J Health Psychol*, 17(2): 244–257.
- [15] Traeger AC, Hübscher M, Henschke N, et al., 2015, Effect of Primary Care-Based Education on Reassurance in Patients with Acute Low Back Pain: Systematic Review and Meta-analysis. *JAMA Intern Med*, 175(5): 733–743.
- [16] Alperstein D, Sharpe L, 2016, The Efficacy of Motivational Interviewing in Adults with Chronic Pain: A Meta-Analysis and Systematic Review. *J Pain*, 17(4): 393–403.
- [17] Lundahl B, Moleni T, Burke BL, et al., 2013, Motivational Interviewing in Medical Care Settings: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Patient Educ Couns*, 93(2): 157–168.
- [18] Rollnick S, Miller WR, Butler CC, 2008, *Motivational Interviewing in Health Care: Helping Patients Change Behavior*, Guilford Publications, New York, 210.
- [19] Sensitivierung [Sensitization], n.d., Spectrum Academic Publishers, Heidelberg, <https://www.spektrum.de/lexikon/neurowissenschaft/sensitivierung/11711>
- [20] Latremoliere A, Woolf CJ, 2009, Central Sensitization: A Generator of Pain Hypersensitivity by Central Neural Plasticity. *J Pain*, 10(9): 895–926.
- [21] Woolf CJ, 2011, Central Sensitization: Implications for the Diagnosis and Treatment of Pain. *Pain*, 152: S2–S15.
- [22] O’Neill TW, Felson DT, 2018, Mechanisms of Osteoarthritis (OA) Pain. *Curr Osteoporos Rep*, 16(5): 611–616.
- [23] Häuser W, Hansen E, Enck P, 2012, Nocebo Phenomena in Medicine: Their Relevance in Everyday Clinical Practice. *Dtsch Arztebl Int*, 109(26): 459–465.
- [24] Main CJ, Williams AC, 2002, Musculoskeletal Pain. *BMJ*, 325(7363): 534–537.
- [25] Shaw WS, Pransky G, Roter DL, et al., 2011, The Effects of Patient-Provider Communication on 3-Month Recovery From Acute Low Back Pain. *J Am Board Fam Med*, 24(1): 16–25.
- [26] Saunders B, Hill JC, Foster NE, et al., 2020, Stratified Primary Care Versus Non-Stratified Care for Musculoskeletal Pain: Qualitative Findings from the Start MSK Feasibility and Pilot Cluster Randomized Controlled Trial. *BMC Fam Pract*, 21(1): 31.
- [27] Main C, Keefe F, Jensen M, et al., 2013, *Fordyce’s Behavioral Methods for Chronic Pain and Illness*, IASP, USA.

- [28] Merki V, Hurni B, Egloff N, 2022, Funktionelle Körperbeschwerden in Praxis und Spital [Functional Physical Complaints in Practice and Hospital]. *Swiss Medical Forum*, 22(0304): 67–71.
- [29] van den Bekerom MP, Struijs PA, Blankevoort L, et al., 2012, What is the Evidence for Rest, Ice, Compression, and Elevation Therapy in the Treatment of Ankle Sprains in Adults? *J Athl Train*, 47(4): 435–443.
- [30] Chimenti RL, Frey-Law LA, Sluka KA, 2018, A Mechanism-Based Approach to Physical Therapist Management of Pain. *Phys Ther*, 98(5): 302–314.
- [31] Babatunde OO, Jordan JL, Van der Windt DA, et al., 2017, Effective Treatment Options for Musculoskeletal Pain in Primary Care: A Systematic Overview of Current Evidence. *PLoS One*, 12(6): e0178621.
- [32] Paige NM, Miake-Lye IM, Booth MS, et al., 2017, Association of Spinal Manipulative Therapy with Clinical Benefit and Harm for Acute Low Back Pain: Systematic Review and Meta-Analysis. *JAMA*, 317(14): 1451–1460.
- [33] Hill JC, Whitehurst DG, Lewis M, et al., 2011, Comparison of Stratified Primary Care Management for Low Back Pain with Current Best Practice (Start Back): A Randomised Controlled Trial. *Lancet*, 378(9802): 1560–1571.
- [34] Nicholas MK, Costa DSJ, Linton SJ, et al., 2020, Implementation of Early Intervention Protocol in Australia for ‘High Risk’ Injured Workers is Associated with Fewer Lost Work Days Over 2 Years Than Usual (Stepped) Care. *J Occup Rehabil*, 30(1): 93–104.
- [35] Lambeek LC, Bosmans JE, Van Royen BJ, et al., 2010, Effect of Integrated Care for Sick Listed Patients with Chronic Low Back Pain: Economic Evaluation Alongside a Randomised Controlled Trial. *BMJ*, 341: c6414.
- [36] Suman A, Schaafsma FG, Buchbinder R, et al., 2017, Implementation of a Multidisciplinary Guideline for Low Back Pain: Process-Evaluation Among Health Care Professionals. *J Occup Rehabil*, 27(3): 422–433.
- [37] Hall AM, Surrency SR, Pike AE, et al., 2019, Physician-Reported Barriers to Using Evidence-Based Recommendations for Low Back Pain in Clinical Practice: A Systematic Review and Synthesis of Qualitative Studies Using the Theoretical Domains Framework. *Implement Sci*, 14(1): 49.
- [38] Kesselring J, Oesch P, 2017, Teamwork in Rehabilitation – It Is Effective but It Must Be Financed. *Swiss Med Wkly*, 147: w14449.
- [39] Traeger AC, Buchbinder R, Elshaug AG, et al., 2019, Care for Low Back Pain: Can Health Systems Deliver? *Bull World Health Organ*, 97(6): 423–433.
- [40] Lima LV, Abner TSS, Sluka KA, 2017, Does Exercise Increase or Decrease Pain? Central Mechanisms Underlying These Two Phenomena. *J Physiol*, 595(13): 4141–4150.
- [41] Galdino G, Romero T, Pinho da Silva JF, et al., 2014, Acute Resistance Exercise Induces Antinociception by Activation of the Endocannabinoid System in Rats. *Anesth Analg*, 119(3): 702–715.
- [42] Hayden JA, Ellis J, Ogilvie R, et al., 2021, Exercise Therapy for Chronic Low Back Pain. *Cochrane Database Syst Rev*, 9(9): Cd009790.
- [43] Hayden JA, Ellis J, Ogilvie R, et al., 2021, Some Types of Exercise Are More Effective Than Others in People with Chronic Low Back Pain: A Network Meta-Analysis. *J Physiother*, 67(4): 252–262.
- [44] Garland EL, Brintz CE, Hanley AW, et al., 2020, Mind-Body Therapies for Opioid-Treated Pain: A Systematic Review and Meta-Analysis. *JAMA Intern Med*, 180(1): 91–105.

- [45] Elbers S, Wittink H, Pool JJM, et al., 2018, The Effectiveness of Generic Self-Management Interventions for Patients with Chronic Musculoskeletal Pain on Physical Function, Self-Efficacy, Pain Intensity and Physical Activity: A Systematic Review and Meta-Analysis. *Eur J Pain*, 22(9): 1577–1596.
- [46] Kamper SJ, Apeldoorn AT, Chiarotto A, et al., 2014, Multidisciplinary Biopsychosocial Rehabilitation for Chronic Low Back Pain. *Cochrane Database Syst Rev*, 2014(9): Cd000963.
- [47] Koele R, Volker G, van Vree F, et al., 2014, Multidisciplinary Rehabilitation for Chronic Widespread Musculoskeletal Pain: Results from Daily Practice. *Musculoskeletal Care*, 12(4): 210–220.
- [48] Brady B, Veljanova I, Chipchase L, 2016, Are Multidisciplinary Interventions Multicultural? A Topical Review of the Pain Literature as It Relates to Culturally Diverse Patient Groups. *Pain*, 157(2): 321–328.
- [49] Qaseem A, McLean RM, O’Gurek D, et al., 2020, Nonpharmacologic and Pharmacologic Management of Acute Pain from Non-Low Back, Musculoskeletal Injuries in Adults: A Clinical Guideline from the American College of Physicians and American Academy of Family Physicians. *Ann Intern Med*, 173(9): 739–748.
- [50] Busse JW, Sadeghirad B, Oparin Y, et al., 2020, Management of Acute Pain From Non-Low Back Musculoskeletal Injuries: A Systematic Review and Network Meta-Analysis of Randomized Trials. *Ann Intern Med*, 173(9): 730–738.
- [51] Bichsel D, Liechti FD, Schlapbach JM, et al., 2021, Cross-Sectional Analysis of Recommendations for the Treatment of Hip and Knee Osteoarthritis in Clinical Guidelines. *Arch Phys Med Rehabil*, 103(3): 559–569.
- [52] Wertli MM, Reich O, Signorell A, et al., 2017, Changes Over Time in Prescription Practices of Pain Medications in Switzerland Between 2006 and 2013: An Analysis of Insurance Claims. *BMC Health Serv Res*, 17(1): 167.
- [53] Haschke M, Liechti ME, 2017, Metamizol: Nutzen und Risiken im Vergleich zu Paracetamol und NSAR [Metamizole: Benefits and Risks Compared to Paracetamol and NSAIDs]. *Swiss Medical Forum*, 17(48): 1067–1073.
- [54] Hsu JR, Mir H, Wally MK, et al., 2019, Clinical Practice Guidelines for Pain Management in Acute Musculoskeletal Injury. *J Orthop Trauma*, 33(5): e158–e82.
- [55] Chang AK, Bijur PE, Esses D, et al., 2017, Effect of a Single Dose of Oral Opioid and Nonopioid Analgesics on Acute Extremity Pain in the Emergency Department: A Randomized Clinical Trial. *JAMA*, 318(17): 1661–1667.
- [56] Pergolizzi Jr JV, Raffa RB, Rosenblatt MH, 2020, Opioid Withdrawal Symptoms, A Consequence of Chronic Opioid Use and Opioid Use Disorder: Current Understanding and Approaches to Management. *J Clin Pharm Ther*, 45(5): 892–903.
- [57] Campbell G, Nielsen S, Larance B, et al., 2015, Pharmaceutical Opioid Use and Dependence among People Living with Chronic Pain: Associations Observed within the Pain and Opioids in Treatment (POINT) Cohort. *Pain Med*, 16(9): 1745–1758.
- [58] Krebs EE, Gravely A, Nugent S, et al., 2018, Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients with Chronic Back Pain or Hip or Knee Osteoarthritis Pain: The SPACE Randomized Clinical Trial. *JAMA*, 319(9): 872–882.
- [59] Chou R, Turner JA, Devine EB, et al., 2015, The Effectiveness and Risks of Long-Term Opioid Therapy for Chronic Pain: A Systematic Review for a National Institutes of Health Pathways to

Prevention Workshop. *Ann Intern Med*, 162(4): 276–286.

- [60] Frank JW, Lovejoy TI, Becker WC, et al., 2017, Patient Outcomes in Dose Reduction or Discontinuation of Long-Term Opioid Therapy: A Systematic Review. *Ann Intern Med*, 167(3): 181–191.
- [61] Fitzcharles MA, Baerwald C, Ablin J, et al., 2016, Efficacy, Tolerability and Safety of Cannabinoids in Chronic Pain Associated with Rheumatic Diseases (Fibromyalgia Syndrome, Back Pain, Osteoarthritis, Rheumatoid Arthritis): A Systematic Review of Randomized Controlled Trials. *Schmerz*, 30(1): 47–61.
- [62] Friedman BW, Irizarry E, Solorzano C, et al., 2017, Diazepam Is No Better Than Placebo When Added to Naproxen for Acute Low Back Pain. *Ann Emerg Med*, 70(2): 169–176.
- [63] Shanthanna H, Gilron I, Rajarathinam M, et al., 2017, Benefits and Safety of Gabapentinoids in Chronic Low Back Pain: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *PLoS Med*, 14(8): e1002369.
- [64] Mason L, Moore RA, Edwards JE, 2004, Topical NSAIDs for Chronic Musculoskeletal Pain: Systematic Review and Meta-Analysis. *BMC Musculoskelet Disord*, 5: 28.
- [65] Moore RA, Derry S, Wiffen PJ, et al., 2015, Overview Review: Comparative Efficacy of Oral Ibuprofen and Paracetamol (Acetaminophen) Across Acute and Chronic Pain Conditions. *Eur J Pain*, 19(9): 1213–1223.
- [66] Towheed TE, Maxwell L, Judd MG, et al., 2006, Acetaminophen for Osteoarthritis. *Cochrane Database Syst Rev*, 2006(1): Cd004257.
- [67] Chaparro LE, Furlan AD, Deshpande A, et al., 2014, Opioids Compared with Placebo or Other Treatments for Chronic Low Back Pain: An Update of the Cochrane Review. *Spine (Phila Pa 1976)*, 39(7): 556–563.

Publisher's note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Appendix

Table S1. Recommendations for the management of musculoskeletal pain

Recommendation	Implementation in practice (examples)
(1) Consider the context of the patient. Use effective communication and empower the patient to make their own decisions.	The presence of family members can be helpful. Let the patient finish speaking and address individual needs.
(2) Screen systematically to identify early risk of serious illness or injury.	Imaging/further investigations should only be performed in patients with red flags or a high likelihood that imaging will affect treatment. Clinical prediction rules (<i>e.g.</i> , Ottawa Ankle Rules for foot sprains or C-spine rules for spinal trauma) with high sensitivity and specificity can support the decision.
(3) Be aware of psychosocial risk factors.	Signs of stress, anxiety, or job loss are proven risk factors of chronic pain.
(4) Avoid imaging procedures.	If there are no warning signals or indications of a serious injury, treatment attempt should be made without prior imaging. Imaging should be performed if there is inadequate treatment or if symptoms worsen.
(5) Physical examination with neurological screening tests; measurement of activity or muscle strength.	A well-founded physical examination shows a serious attitude toward the patient's pain.
(6) Measurement with validated measuring instruments.	There are validated and inexpensive tests that can be used to get a good insight into the course and prognosis of patient with little effort (<i>e.g.</i> , 1-minute sit-to-stand test).
(7) Educating and informing patients about problems and treatment options.	Use metaphors, images, graphics, models, instructional videos, and brochures to help explain complex issues without using medical jargons.
(8) Counseling to be physically active.	Find out how and when the patient engages in physical activity to manage his/her pain.
(9) Use manual techniques from medicine, chiropractic, or osteopathy based on other evidence-based measures.	Brief manual techniques can help but should always be accompanied by instruction during self-application or home practice.
(10) Non-surgical options are given priority when counseling patients (except in acute emergencies).	In the case of non-surgical measures, take the patient's inclinations into account.
(11) Consider continuing or resuming work despite persistent pain.	Do not be afraid to bring up the subject of work during consultation, ask whether the patient has already spoken to his/her employer, and clarify whether he/she needs non-medical support to reintegrate into everyday private and professional life.
(12) Consider culture-specific aspects.	Cultural differences in the perception of pain should be taken into account in treatment.
(13) Show interest and take time to understand patients with chronic and persistent somatoform pain in order to come up with an optimal treatment plan.	Identify individual risk factors to ensure targeted therapy and explain the various treatment methods to lower expectations of analgesics and imaging.

(Continued on next page)

(Continued from previous page)

Recommendation	Implementation in practice (examples)
(14) Formulate common treatment goals and a treatment plan.	Since pain often cannot be relieved completely, a joint formulation of individual and realistic treatment goals, which often have nothing to do with pain relief, is essential.

Table S2. Pharmacological measures for musculoskeletal pain

	Acute	Chronic	Most important CI/SE	Reference
Topical NSAIDs	<ul style="list-style-type: none"> • First choice • Reduces pain and improves physical function • Increases patient satisfaction with the treatment 	<ul style="list-style-type: none"> • First choice 	CI: Known hypersensitivity/allergies, open wound, pregnancy (3rd trimester), lactation SE: Dermatitis, photosensitization, systemic side effects with long-term and large-scale use	CPG [12] SR [31] CPG [49] SR [64]
Oral NSAIDs	<ul style="list-style-type: none"> • Second choice or in combination with topical NSAIDs 	<ul style="list-style-type: none"> • First choice 	CI: Allergies, GI ulcer, liver and renal insufficiency, pregnancy (especially 3rd trimester), lactation SE: Acute renal failure, hypertension, increased risk of cardiovascular events, GI problems (ulcer/gastritis)	CPG [12] SR [31] CPG [49] SR [64]
Paracetamol	Controversial recommendations: <ul style="list-style-type: none"> • Short-term (1–7 days) • Use in combination with other analgesic drugs • Not recommended (non-specific lumbar back pain) 	<ul style="list-style-type: none"> • Controversial, as less effective than NSAIDs • Significantly reduces pain statistically compared to placebo • Clinical significance is unclear 	CI: Allergies, severe hepatic impairment, acute hepatitis, decompensated liver disease, Gilbert’s syndrome SE: Allergic reactions, hepatopathy with increased transaminases and cholestasis parameters	CPG [12] SR [31] CPG [49] SR [50] SR [65] SR [66]
Metamizole	<ul style="list-style-type: none"> • No studies of its efficacy for musculoskeletal pain 	<ul style="list-style-type: none"> • No studies of its efficacy for musculoskeletal pain 	CI: Allergies, porphyria, G6PD deficiency, hematopoietic disorders, pregnancy (1st and 3rd trimester), lactation SE: Allergic reaction, hypotension on intravenous administration, agranulocytosis, thrombocytopenia	
Corticosteroid injection	<ul style="list-style-type: none"> • Short term; effective for moderate to severe shoulder and knee pain • Not recommended for neck or back pain 	<ul style="list-style-type: none"> • Short term; effective for moderate to severe shoulder and knee pain • Not recommended for neck or back pain 	CI: Pregnancy, lactation SE: Risk of infection from injection, adrenal suppression (especially with repetitive use), intestinal bleeding	SR [31]

(Continued on next page)

(Continued from previous page)

	Acute	Chronic	Most important CI/SE	Reference
Weak opioids	<ul style="list-style-type: none"> Short-term; recommended for low back pain when NSAIDs are contraindicated or symptoms do not improve 	<ul style="list-style-type: none"> More effective compared to placebo for short-term use Short-term; recommended for low back pain when NSAIDs are contraindicated or symptoms do not improve More side effects, without improved clinical endpoints in long-term use, compared to non-opioids; worsen quality of life 	CI: Hypersensitivity/allergy, acute intoxication, uncontrolled epilepsy, on MOA inhibitors (interactions), pregnancy, lactation SE: Dizziness, nausea, vomiting, constipation, dry mouth, headache, hyperhidrosis, exhaustion; lower seizure threshold with high doses of tramadol	CPG [12] RCT [58] SR [67]
Strong opioids	<ul style="list-style-type: none"> Reduces pain in comparison to placebo, but no greater than NSAIDs Use with caution due to side effects (short-term short-acting opioids if other pain medications are insufficient) 	<ul style="list-style-type: none"> Not recommended More effective compared to placebo for short-term use Compared with other pain medications, more side effects, without improved clinical endpoints; quality of life deteriorates Reduction or discontinuation may improve severity of pain (opioid-induced hyperalgesia), function, and quality of life 	CI: Severe respiratory depression with hypoxia or hypercapnia, severe COPD, cor pulmonale, severe asthma, paralytic ileus, pregnancy, lactation SE: Dizziness, headache, tremor, sluggishness, constipation, nausea, vomiting, dyspnea, bronchospasm, pruritus, fatigue	SR [50] CPG [54] RCT [55] RCT [58] SR [60] SR [67]
Cannabis	<ul style="list-style-type: none"> No studies on its efficacy for musculoskeletal pain 	<ul style="list-style-type: none"> No pain reduction by nabilone compared with placebos in patients with fibromyalgia syndrome Chronic back pain 	CI: Hypersensitivity to cannabis extract, suicidality or suicidal thoughts, known or suspected medical history or family history of schizophrenia or others psychosis, lactation SE: Drowsiness, dry mouth, euphoria, ataxia, headaches, and difficulty concentrating	SR [61]

(Continued on next page)

(Continued from previous page)

	Acute	Chronic	Most important CI/SE	Reference
Benzodiazepine	<ul style="list-style-type: none"> No improvement in functional outcomes or pain in patients with acute, non-traumatic, non-radicular low back pain with naproxen + diazepam compared to naproxen + placebo 	<ul style="list-style-type: none"> No studies on its efficacy for musculoskeletal pain 	CI: Myasthenia gravis, severe respiratory failure, sleep apnea, severe hepatic impairment, severe renal impairment, shock, collapse, coma; acute intoxication with alcohol, psychotropic drugs, sleeping pills, or painkillers; addiction, pregnancy, lactation SE: Sedation, fatigue, ataxia, confusion, depression, muscle weakness	RCT [62]
Gabapentinoids	<ul style="list-style-type: none"> No studies on its efficacy for musculoskeletal pain 	<ul style="list-style-type: none"> Gabapentin reduces pain slightly, especially neuropathic pain Pregabalin less effective compared to an analgesic 	CI: Pregnancy, lactation SE: Dizziness, tiredness, difficulty thinking, visual disturbances	SR [63]

*List as an example and not exhaustive. Abbreviations: CI, contraindications; COPD, chronic obstructive pulmonary disease; CPG, clinical practice guideline; G6PD, glucose-6-phosphate dehydrogenase; GI, gastrointestinal; NSAIDs, non-steroidal anti-inflammatory drugs; RCT, randomized controlled trials; SE, side effects; SR, systematic literature reviews.