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Evidence for peripheral neuroinflammation after acute whiplash

Colette Ridehalgh, Joel Fundaun, Stephen Bremner, Mara Cercignani, Soraya Koushesh, Rupert Young, Alex Novak, Jane Greening, Annina B Schmid, Andrew Dilley Pain. 2025 Mar 4. doi: 10.1097/j.pain.000000000003560.

Abstract:

Whiplash injury is associated with high socioeconomic costs and poor prognosis. Most people are classified as having whiplash-associated disorder grade II (WADII), with neck complaints and musculoskeletal signs, in the absence of frank neurological signs. However, evidence suggests that there is a subgroup with underlying nerve involvement in WADII, such as peripheral neuroinflammation. This study aimed to investigate the presence of neuroinflammation in acute WADII using T2-weighted magnetic resonance imaging of the brachial plexus, dorsal root ganglia and median nerve, and clinical surrogates of neuroinflammation: heightened nerve mechanosensitivity (HNM), raised serum inflammatory mediators, and somatosensory hyperalgesia. One hundred twenty-two WADII participants within 4 weeks of whiplash and 43 healthy controls (HCs) were recruited. Magnetic resonance imaging T2 signal ratio was increased in the C5 root of the brachial plexus and the C5-C8 dorsal root ganglia in WADII participants compared with HCs but not in the distal median nerve trunk. Fifty-five percent of WADII participants had signs of HNM. Inflammatory mediators were also raised compared with HCs, and 47% of WADII participants had somatosensory changes on quantitative sensory testing. In those WADII individuals with HNM, there was hyperalgesia to cold and pressure and an increased proportion of neuropathic pain. Many people with WADII had multiple indicators of neuroinflammation. Overall, our results present a complex phenotypic profile for acute WADII and provide evidence suggestive of peripheral neuroinflammation in a subgroup of individuals. The results suggest that there is a need to reconsider the management of people with WADII.

Analgesic effects of non-surgical and non-interventional treatments for low back pain: a systematic review and meta-analysis of placebocontrolled randomised trials

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BMJ Evid Based Med. 2025 Mar 18:bmjebm-2024-112974. doi: 10.1136/bmjebm-2024-112974.

Abstract:

Objectives: To investigate the efficacy of non-surgical and noninterventional treatments for adults with low back pain compared with placebo.

Eligibility criteria: Randomised controlled trials evaluating non-surgical and non-interventional treatments compared with placebo or sham in adults (≥18 years) reporting non-specific low back pain.

Information sources: MEDLINE, CINAHL, EMBASE, PsychInfo and Cochrane Central Register of Controlled Trials were searched from inception to 14 April 2023.

Risk of bias: Risk of bias of included studies was assessed using the 0 to 10 PEDro Scale.

Synthesis of results: Random effects meta-analysis was used to estimate pooled effects and corresponding 95% confidence intervals on outcome pain intensity (0 to 100 scale) at first assessment post-treatment for each treatment type and by duration of low back pain-(sub)acute (<12 weeks) and chronic (≥12 weeks). Certainty of the evidence was assessed using the Grading of Recommendations Assessment (GRADE) approach.

Results: A total of 301 trials (377 comparisons) provided data on 56 different treatments or treatment combinations. One treatment for acute low back pain (non-steroidal anti-inflammatory drugs (NSAIDs)), and five treatments for chronic low back pain (exercise, spinal manipulative therapy, taping, antidepressants, transient receptor potential vanilloid 1 (TRPV1) agonists) were efficacious; effect sizes were small and of moderate certainty. Three treatments for acute low back pain (exercise,

glucocorticoid injections, paracetamol), and two treatments for chronic low back pain (antibiotics, anaesthetics) were not efficacious and are unlikely to be suitable treatment options; moderate certainty evidence. Evidence is inconclusive for remaining treatments due to small samples, imprecision, or low and very low certainty evidence. **Conclusions:** The current evidence shows that one in 10 non-surgical and non-interventional treatments for low back pain are efficacious, providing only small analgesic effects beyond placebo. The efficacy for the majority of treatments is uncertain due to the limited number of randomised participants and poor study quality. Further high-quality, placebo-controlled trials are warranted to address the remaining uncertainty in treatment efficacy along with greater consideration for placebo-control design of non-surgical and non-interventional treatments.

Sustained versus repetitive standing trunk extension results in greater spinal growth and pain improvement in back pain:A randomized clinical trial

Jeremy J Harrison, Jean-Michel Brismée, Phillip S Sizer Jr, Brent K Denny, Stéphane Sobczak J Back Musculoskelet Rehabil. 2024;37(2):395-405. doi: 10.3233/BMR-230118.

Abstract:

Background: McKenzie standing trunk extension exercises have been used for the management of low back pain (LBP). However, no study to date has investigated the effect of standing trunk extension postures on spinal height and clinical outcomes.

Objective: To evaluate in subjects with LBP following a period of trunk loading how spinal height, pain, symptoms' centralization and function outcome measures respond to two standing postures interventions: (1) repetitive trunk extension (RTE) and (2) sustained trunk extension (STE). **Methods:** A consecutive sample of convenience of people with LBP were recruited to participate in 2-session physical therapy using either RTE or STE in standing.

Results: Thirty participants (18 women) with a mean age of 53 ± 17.5 years completed the study. The first session resulted in spinal height increase (spinal growth) of 2.07 \pm 1.32 mm for the RTE intervention and 4.54 \pm 1.61 mm for the STE group (p< 0.001; ES = 1.67), while the second session (2-week following the first session) resulted in spinal growth of 2.39 \pm 1.46 mm for the RTE group and 3.91 \pm 2.06 mm for the STE group (p= 0.027; ES = 0.85). The STE group presented with the larger reduction in most pain from 6 to 2 as compared to the RTE group from 6 to 4 between Session 1 and Session 2 (p< 0.001). There was no difference between the groups in

Modified Oswestry score and symptoms centralization (p= 0.88 and p= 0.77, respectively).

Conclusion: People with LBP experienced greater spine growth and improvements of pain during standing STE as compared to RTE. People with LBP could use such postures and movements to alleviate their LBP and improve spine height while in a weight bearing position.

Low back pain and sitting time, posture and behavior in office workers: A scoping review

Nuray Alaca, Ali Ömer Acar, Sergen Öztürk J Back Musculoskelet Rehabil. 2025 Mar 20:10538127251320320. doi: 10.1177/10538127251320320.

Abstract:

Background: Office workers spend approximately two-thirds of their daily work time in a sitting position.

Objective: This scoping review aimed to identify and categorize key themes and knowledge gaps in research on how sitting time, posture, and behavior affect the risk of low back pain among office workers.

Methods: The authors conducted a comprehensive literature search in electronic databases [MEDLINE [via PubMed], SCOPUS, CINAHL, PEDro, and CENTRAL] from inception to March 2024, resulting in 22 studies involving 7814 participants. The methodological quality of these studies was assessed using the Mixed Methods Appraisal Tool (MMAT).

Results: Seventeen studies [77%] were rated as high quality, four studies [18%] as moderate quality, and one study [5%] as low quality. Thirteen studies assessed sitting time, ten assessed sitting posture, and thirteen assessed sitting behavior. Among the studies investigating sitting time, five showed no relationship with low back pain (LBP) prevalence, while eight demonstrated a relationship with LBP prevalence. For studies exploring sitting posture, seven found a relationship with LBP. Regarding studies on sitting behavior, only one showed no relationship between LBP prevalence, while twelve indicated a relationship.

Conclusions: Longer sitting time, poor sitting posture, fewer breaks and more static sitting in sitting behavior, were found to be associated with LBP. The strongest evidence for an association with LBP was found for sitting behavior. When considering workplace ergonomics and interventions for LBP, it is advisable to consider all factors, including sitting, posture and behavior.

Effectiveness of reducing tendon compression in the rehabilitation of insertional Achilles tendinopathy: a randomised clinical trial

Lauren Pringels, Robbe Capelleman, Aäron Van den Abeele, Arne Burssens, Guillaume Planckaert, Evi Wezenbeek, Luc Vanden Bossche Br J Sports Med. 2025 Feb 26:bjsports-2024-109138. doi: 10.1136/bjsports-2024-109138.

Abstract:

Objective: To assess the effectiveness of low tendon compression rehabilitation (LTCR) versus high tendon compression rehabilitation (HTCR) for treating patients with insertional Achilles tendinopathy. Methods: In an investigator-blinded, stratified randomised trial, 42 sportactive patients (30 males and 12 females; age 45.8±8.2 years) with chronic (> 3 months) insertional Achilles tendinopathy were allocated in a 1:1 ratio to receive LTCR or HTCR. Both rehabilitation protocols consisted of a progressive 4-stage tendon-loading programme, including isometric, isotonic, energy-storage and release and sport-specific exercises. The LTCR programme was designed to control Achilles tendon compression by limiting ankle dorsiflexion during exercise, eliminating calf stretching and incorporating heel lifts. The primary outcome was the Victorian Institute of Sports Assessment-Achilles (VISA-A) score at 12 and 24 weeks, which measures tendon pain and function and was analysed on an intention-totreat basis using a linear mixed model. Significance was accepted when p<0.05.

Results: 20 patients were randomised to the LTCR group and 22 to the HTCR group. Improvement in VISA-A score was significantly greater for LTCR compared with HTCR after 12 weeks (LTCR=24.4; HTCR=12.2; mean between-group difference=12.9 (95% CI: 6.2 to 19.6); p<0.001) and after 24 weeks (LTCR=29.0; HTCR=19.3; mean between-group difference=10.4 (95% CI: 3.7 to 17.1); p<0.001). These differences exceeded the minimal clinically important difference of 10.

Conclusions: In sport-active patients with insertional Achilles tendinopathy, LTCR was more effective than HTCR in improving tendon pain and function at 12 and 24 weeks. Consequently, LTCR should be considered in the treatment of insertional Achilles tendinopathy.

Inter-rater reliability of Mechanical Diagnosis and Therapy (MDT) in evaluating and classifying chronic pelvic pain syndrome

Di Wu, Catherine Bednarczyk, Adriana RamonFigueroa, Helen Zhu, Meridith Geer, Richard Rosedale, Shawn M Robbins J Man Manip Ther. 2025 Mar 17:1-8. doi: 10.1080/10669817.2025.2475456.

Abstract:

Introduction: Chronic pelvic pain syndrome (CPPS) involves complex interactions between the musculoskeletal system, nervous system, and psychosocial factors. A major challenge in managing CPPS is the lack of reliable assessment and classification systems. The Mechanical Diagnosis and Therapy (MDT) is a widely used and reliable classification system for assessing and managing painful musculoskeletal conditions affecting the spine and extremities. This study's primary objective was to assess the inter-rater reliability of the MDT assessment in diagnosing CPPS using clinical vignettes. Secondary objectives included determining the prevalence of MDT classification categories.

Methods: Five MDT clinicians classified clinical vignettes into three categories: 1) Spinal Derangement, 2) Pelvic Floor Contractile Dysfunction, or 3) MDT OTHER subgroups. The vignettes were developed from the McKenzie Pelvic Pain Assessment Form. Inter-rater reliability among clinicians was calculated using the Fleiss kappa statistic with 95% confidence intervals, and Cohen's kappa examined reliability between pairs of raters.

Results: A total of 76 vignettes were developed (40 females and 36 males). Good inter-rater reliability was found among clinicians (Fleiss kappa = 0.616, 95% CI = 0.598-0.633, p < 0.001). Inter-rater reliability was higher when classifying female vignettes (Fleiss kappa = 0.658, 95% CI = 0.634, 0.682) than male vignettes (Fleiss kappa = 0.546, 95% CI = 0.519, 0.573). The most common classification was Spinal Derangement (57%), followed by MDT OTHER subgroups (26%) and Pelvic Floor Contractile Dysfunction (17%).

Conclusions: The study indicates good inter-rater reliability among MDT clinicians in classifying pelvic pain syndrome. However, clinical vignettes may not fully capture the complexities of real participant interactions, potentially inflating agreement. Future studies should incorporate direct observation of real participant encounters alongside clinical vignettes to improve validity.

Commonly used interventional procedures for non-cancer chronic spine pain: a clinical practice guideline

Jason W Busse, Stéphane Genevay, Arnav Agarwal, Christopher J Standaert, Kevin Carneiro, Jason Friedrich, Manuela Ferreira, Hilde Verbeke, Jens Ivar Brox, Hong Xiao, Jasmeer Singh Virdee, Janet Gunderson, Gary Foster, Conrad Heegsma, Caroline F Samer, Matteo Coen, Gordon H Guyatt, Xiaoqin Wang, Behnam Sadeghirad, Faheem Malam, Dena Zeraatkar, Per O Vandvik, Ting Zhou, Feng Xie, Reed A C Siemieniuk, Thomas Agoritsas BMJ. 2025 Feb 19:388:e079970. doi: 10.1136/bmj-2024-079970.

Abstract:

Clinical question: What is the comparative effectiveness and safety of commonly used interventional procedures (such as spinal injections and ablation procedures) for chronic axial and radicular spine pain that is not associated with cancer or inflammatory arthropathy?

Current practice: Chronic spine pain is a common, potentially disabling complaint, for which clinicians often administer interventional procedures. However, clinical practice guidelines provide inconsistent recommendations for their use.

Recommendations: For people living with chronic axial spine pain (\geq 3 months), the guideline panel issued strong recommendations against: joint radiofrequency ablation with or without joint targeted injection of local anaesthetic plus steroid; epidural injection of local anaesthetic, steroids, or their combination; joint-targeted injection of local anaesthetic, steroids, or their combination; and intramuscular injection of local anaesthetic with or without steroids. For people living with chronic radicular spine pain (\geq 3 months), the guideline panel issued strong recommendations against: dorsal root ganglion radiofrequency with or without epidural injection of local anaesthetic or local anaesthetic plus steroids; and epidural injection of local anaesthetic, steroids, or their combination radiofrequency with or without epidural injection of local anaesthetic, steroids, or local anaesthetic or local anaesthetic plus steroids; and epidural injection of local anaesthetic, steroids, or their combination.

How this guideline was created: An international guideline development panel including four people living with chronic spine pain, 10 clinicians with experience managing chronic spine pain, and eight methodologists, produced these recommendations in adherence with standards for trustworthy guidelines using the GRADE approach. The MAGIC Evidence Ecosystem Foundation provided methodological support. The guideline

panel applied an individual patient perspective when formulating recommendations.

The evidence: These recommendations are informed by a linked systematic review and network meta-analysis of randomised trials and a systematic review of observational studies, summarising the current body of evidence for benefits and harms of common interventional procedures for axial and radicular, chronic, non-cancer spine pain. Specifically, injection of local anaesthetic, steroids, or their combination into the cervical or lumbar facet joint or sacroiliac joint; epidural injections of local anaesthetic, steroids, or their combination; radiofrequency of dorsal root ganglion; radiofrequency denervation of cervical or lumbar facet joints or the sacroiliac joint; and paravertebral intramuscular injections of local anaesthetic, steroids, or their combination.

Understanding the recommendations: These recommendations apply to people living with chronic spine pain (≥3 months duration) that is not associated with cancer or inflammatory arthropathy and do not apply to the management of acute spine pain. Further research is warranted and may alter recommendations in the future: in particular, whether there are differences in treatment effects based on subtypes of chronic spine pain, establishing the effectiveness of interventional procedures currently supported by low or very low certainty evidence, and effects on poorly reported patient-important outcomes (such as opioid use, return to work, and sleep quality).

Stratified health care for low back pain using the STarT Back approach: holy grail or doomed to fail?

Peter Croft, Jonathan C Hill, Nadine E Foster, Kate M Dunn, Danielle A van der Windt Pain. 2024 Dec 1;165(12):2679-2692. doi: 10.1097/j.pain.00000000003319.

Abstract:

There have been at least 7 separate randomised controlled trials published between 2011 and 2023 that have examined primary care for nonspecific low back pain informed by the STarT Back approach to stratified care based on risk prediction, compared with care not informed by this approach. The results, across 4 countries, have been contrasting-some demonstrating effectiveness and/or efficiency of this approach, others finding no benefits over comparison interventions. This review considers possible explanations for the differences, particularly whether this is related to poor predictive performance of the STarT Back risk-prediction tool or to variable degrees of success in implementing the whole STarT Back approach (subgrouping and matching treatments to predicted risk of poor outcomes) in different healthcare systems. The review concludes that although there is room for improving and expanding the predictive value of the STarT Back tool, its performance in allocating individuals to their appropriate risk categories cannot alone explain the variation in results of the trials to date. Rather, the learning thus far suggests that challenges in implementing stratified care in clinical practice and in changing professional practice largely explain the contrasting trial results. The review makes recommendations for future research, including greater focus on studying facilitators of implementation of stratified care and developing better treatments for patients with nonspecific low back pain at high risk of poor outcomes.

The presence and prognosis of nerve pathology following whiplash injury: a prospective cohort study

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Brain. 2025 Mar 5:awaf088. doi: 10.1093/brain/awaf088.

Abstract:

Whiplash Associated Disorders (WAD) affect 20-50 million individuals globally each year, with up to 50% developing persistent pain. WAD grade II (WADII) is the most common type and is characterised by neck symptoms and musculoskeletal signs without apparent nerve injury on routine diagnostic testing. However, emerging evidence suggests nerve pathology may be present in some people with WADII. This longitudinal cohort study aimed to comprehensively investigate the presence, temporal patterns, and prognostic value of nerve pathology and neuropathic pain in acute WADII. A prospective longitudinal cohort study was conducted with 129 acute participants with WADII (median age 36.0 years, 58% female) and 36 healthy controls (median age 39.0 years, 61% female). Participants with WADII were recruited within four weeks of injury from local emergency departments. Data collection included bedside neurological assessments, quantitative sensory testing (QST), intraepidermal nerve fibre density, and

serum neurofilament light chain (NfL) concentrations. Follow-up assessments were conducted 6-months after injury. Signs of neuropathic pain were present in 65% (84/129) acutely and persisted in 32% (21/66) 6months post-injury. Bedside neurological assessment revealed somatosensory loss of function was present in 54% (70/129) acutely reducing to 25% (17/67) 6-months post-injury. QST demonstrated significantly reduced cold, warm, thermal sensory limen, mechanical, and vibration detection thresholds in acute WADII compared to controls (d>0.47). Acute loss of function in at least one QST parameter was present in 67.6% (85/126) of WADII. At 6-months, participants with WADII showed persistent hypoaesthesia to warm, thermal sensory limen, and mechanical detection thresholds, and decreased mechanical pain and pressure pain sensitivity compared to controls (d>0.44). These functional neurological changes were accompanied by elevated serum neurofilament light chain levels in acute WADII compared to controls (d=-0.52 (95% confidence interval -0.94, -0.10). Intraepidermal nerve fibre densities at the index finger were not significantly different between groups. However, dermal MBP+/PGP+ myelinated nerve bundles at the index finger were reduced 6months post-injury in WADII compared to controls (d=0.69 (0.26, 1.11). Multivariable linear regression suggested bedside tests for hypoaesthesia at the index finger were prognostic for whiplash-related upper quadrant pain 6-months post-injury (r2=0.13, p=0.02). In conclusion, two-thirds of participants with acute WADII initially exhibited signs of neuropathic pain and nerve pathology. At the 6-month follow-up, neuropathic pain persisted in one-third of participants with WADII, while nerve pathology persisted in two-thirds. These findings challenge the traditional musculoskeletal classification of WADII and underscore the need for targeted neurological assessments and treatment.