

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

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Description: The American College of Physicians (ACP) and American Academy of Family Physicians (AAFP) developed this guideline to provide clinical recommendations on nonpharmacologic and pharmacologic management of acute pain from non-low back, musculoskeletal injuries in adults in the outpatient setting. The guidance is based on current best available evidence about benefits and harms, taken in the context of costs and patient values and preferences. This guideline does not address noninvasive treatment of low back pain, which is covered by a separate ACP guideline that has also been endorsed by AAFP.

Methods: This guideline is based on a systematic evidence review on the comparative efficacy and safety of nonpharmacologic and pharmacologic management of acute pain from non-low back, musculoskeletal injuries in adults in the outpatient setting and a systematic review on the predictors of prolonged opioid use. We evaluated the following clinical outcomes using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system: pain (at ≤ 2 hours and at 1 to 7 days), physical function, symptom relief, treatment satisfaction, and adverse events.

Target Audience and Patient Population: The target audience is all clinicians, and the target patient population is adults with acute pain from non-low back, musculoskeletal injuries.

Recommendation 1: ACP and AAFP recommend that clinicians treat patients with acute pain from non-low back, musculoskeletal injuries with topical nonsteroidal anti-inflammatory drugs (NSAIDs) with or without menthol gel as first-line therapy to reduce or relieve

symptoms, including pain; improve physical function; and improve the patient's treatment satisfaction (Grade: strong recommendation; moderate-certainty evidence).

Recommendation 2a: ACP and AAFP suggest that clinicians treat patients with acute pain from non-low back, musculoskeletal injuries with oral NSAIDs to reduce or relieve symptoms, including pain, and to improve physical function, or with oral acetaminophen to reduce pain (Grade: conditional recommendation; moderate-certainty evidence).

Recommendation 2b: ACP and AAFP suggest that clinicians treat patients with acute pain from non-low back, musculoskeletal injuries with specific acupressure to reduce pain and improve physical function, or with transcutaneous electrical nerve stimulation to reduce pain (Grade: conditional recommendation; low-certainty evidence).

Recommendation 3: ACP and AAFP suggest against clinicians treating patients with acute pain from non-low back, musculoskeletal injuries with opioids, including tramadol (Grade: conditional recommendation; low-certainty evidence).

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Musculoskeletal injuries are common and are most frequently treated in outpatient settings. In 2010, they accounted for more than 65 million health care visits in the United States and 4 of 5 injuries that were treated in a physician's office were musculoskeletal (1). The estimated annual cost of treating musculoskeletal injuries was \$176.1 billion in 2010 (1).

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Acute musculoskeletal pain lasts less than 4 weeks and includes strains and sprains, soft tissue injuries, whiplash, and various other conditions ranging from nonsurgical fractures to contusions (2). Numerous treatment options exist, including nonpharmacologic and pharmacologic interventions (nonopioid and opioid) (3–6). In the United States, approximately one fifth of patients presenting with pain in the outpatient setting receive an opioid prescription (7) and opioid prescriptions for acute musculoskeletal injuries, such as ankle sprains, are common (8, 9). As of 2015, 2 million persons had an opioid use disorder involving prescription opioids (10), although prescribing rates have decreased in recent years.

GUIDELINE FOCUS AND TARGET POPULATION

The purpose of this guideline from the American College of Physicians (ACP) and American Academy of Family Physicians (AAFP) is to present clinical recommendations on nonpharmacologic and pharmacologic management of acute, non-low back, musculoskeletal injuries in adults in outpatient settings based on the best available evidence of the benefits and harms of treatment and consideration of costs and patient values and preferences. This guideline does not address non-invasive treatment of low back pain, which is covered by a separate ACP guideline that was endorsed by AAFP (6).

The target audience for this guideline is all clinicians, and the target patient population is adults with acute pain from non-low back, musculoskeletal injuries.

METHODS

This guideline was jointly developed by ACP's Clinical Guidelines Committee (CGC) and representatives from AAFP according to ACP's guideline development process, details of which can be found in the methods papers (11, 12). This guideline is based on 2 systematic evidence reviews: a network meta-analysis on the comparative efficacy and safety of nonpharmacologic and pharmacologic treatments for acute musculoskeletal injuries (2) and a systematic review on the predictors of prolonged opioid use (13). Both were done by an evidence review team at McMaster University and funded by the National Safety Council (2, 13), which had no role in the development, review, or approval of this guideline or the 2 systematic evidence reviews.

Systematic Evidence Reviews

The accompanying systematic evidence reviews (2, 13) and the **Appendix** (available at [Annals.org](https://www.annals.org)) provide details and methods. Reviewers searched several databases for randomized controlled trials (RCTs) and reference lists from included trials and guidelines. They selected studies published between database inception and 2 January 2020 that assessed adults aged 18 years or older with acute musculoskeletal pain in the outpatient setting. Acute pain was defined as lasting less than 4 weeks, and studies assessing the treatment of low back pain were excluded.

Main Outcomes

The network meta-analysis evaluated the following outcomes: pain relief (at ≤ 2 hours and at 1 to 7 days); physical function; symptom relief; treatment satisfaction; and gastrointestinal (GI), dermatologic, and neurologic adverse events. Pain relief and function were reported as mean score differences on a 10-cm visual analogue scale (VAS) using a minimally important difference of 1 cm, whereas symptom relief, treatment satisfaction, and adverse events were reported as dichotomous outcomes. Definitions of treatment satisfaction and symptom relief varied across studies and are summarized in detail in the supplement of the network meta-analysis (2). Treatment satisfaction was typically defined as the patient's overall assessment of treatment satisfaction or efficacy (for example, very satisfied or satisfied vs. very unsatisfied or unsatisfied, or good to excellent vs. otherwise). Symptom relief was commonly defined as reaching full resolution of symptoms (for example, no pain, symptom-free, or full relief) or as a marked response to treatment (for example, $\geq 50\%$ reduction in pain score). A second review identified risk factors for prolonged opioid use after a prescription to treat acute musculoskeletal pain (13).

Values and Preferences

The CGC searched several databases (Trip, Epistemonikos, Cochrane Central Register of Controlled Trials, and PubMed) to identify systematic reviews on values and preferences for the management of acute pain. The development of this guideline also included perspectives, values, and preferences of 2 CGC members who represent the public and the CGC Public Panel, who provided comments on the guideline.

Costs

The CGC searched for fair prices of the included interventions via Healthcare Bluebook. If no fair price was publicly available, costs were sourced from the Medicare Physician Fee Schedule (national average, health care professional, and nonfacility payment).

Evidence to Recommendations

Using GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology (14), the CGC based this guideline on an assessment of the benefits and harms of the interventions and consideration of costs and patient values and preferences (**Figure 1**). The tables in **Supplement 1** (available at [Annals.org](https://www.annals.org)) illustrate the GRADE evidence-to-decision framework supporting the recommendations. When evaluating the evidence on benefits and harms, the CGC reviewed results from both the direct evidence and the network meta-analysis and used the highest-certainty evidence that was available regardless of whether it was derived from a direct or network estimate.

Peer Review

The guideline underwent a peer review process through the journal and was posted online for comments from ACP Regents and ACP Governors, who represent internal medicine and its subspecialty physician members at the national and international levels. The

guideline was also reviewed by members of AAFP's Commission on Health of the Public and Science.

SUMMARY OF THE EVIDENCE

The network meta-analysis included 207 trials comprising 32 959 patients; the median of mean patient ages was 34 years (interquartile range, 28 to 39 years). Causes of acute pain varied: 48% of studies included a mix of musculoskeletal injuries, 29% enrolled patients with sprains, 6% enrolled those with whiplash, 5% enrolled those with muscle strains, and the remaining trials included various other injuries ranging from nonsurgical fractures to contusions (2). Twenty-nine percent of studies enrolled persons with isolated ankle injuries, 26% various injuries, 11% neck injuries, 9% upper- and lower-limb injuries, and 7% isolated upper-limb injuries; 7% did not specify a location, and the remaining studies enrolled those with isolated injuries to the hamstring muscle, knee, lower limb, hip, elbow, chest, or ribs. The median average pain score for patients at baseline was 6.49 cm on a 10-cm VAS (2). The systematic review on predictors of prolonged use included 13 observational studies with 13 263 393 participants, including those with work injuries, ankle sprains, low back pain, or several acute pain complaints. Definitions of prolonged use varied across studies.

Benefits of Nonpharmacologic and Pharmacologic Treatments Versus Placebo Pain Relief at Less Than 2 Hours

Evidence was gathered from 28 RCTs with 4464 patients (2).

Nonpharmacologic Treatments. Moderate-certainty evidence showed that on a 10-cm VAS, massage therapy reduced pain at less than 2 hours (weighted mean differ-

ence [WMD], -0.70 cm [95% CI, -1.27 to -0.13 cm]). Low-certainty evidence showed that specific acupressure (WMD, -1.59 cm [CI, -2.52 to -0.66 cm]), joint manipulation therapy (WMD, -1.75 cm [CI, -2.68 to -0.81 cm]), and transcutaneous electrical nerve stimulation (TENS) (WMD, -1.94 cm [CI, -2.90 to -0.98 cm]) reduced pain at less than 2 hours compared with placebo. Low-certainty evidence showed no statistically significant difference in pain at less than 2 hours between nonspecific acupressure and placebo.

Pharmacologic Treatments. High-certainty evidence showed that on a 10-cm VAS, acetaminophen plus opioids reduced pain at less than 2 hours (WMD, -0.50 cm [CI, -1.00 to -0.01 cm]), although the effect was small and based on a single study. Moderate-certainty evidence showed that the following interventions also reduced pain at less than 2 hours compared with placebo: acetaminophen alone (WMD, -1.03 cm [CI, -1.82 to -0.24 cm]), acetaminophen plus oral diclofenac (WMD, -1.11 cm [CI, -2.00 to -0.21 cm]), oral nonsteroidal anti-inflammatory drugs (NSAIDs) (WMD, -0.93 cm [CI, -1.49 to -0.37 cm]), topical NSAIDs (WMD, -1.02 cm [CI, -1.64 to -0.39 cm]), and topical NSAIDs plus menthol gel (WMD, -1.68 cm [CI, -3.09 to -0.27 cm]). Low-certainty evidence showed that a single dose of transbuccal fentanyl (WMD, -3.52 cm [CI, -4.99 to -2.04 cm]) reduced pain at less than 2 hours compared with placebo; however, the direct evidence was based on a small, single-center study (*n* = 60) that included mostly patients with severe pain (suspected fractures). Low-certainty evidence also showed that acetaminophen plus ibuprofen plus codeine (WMD, -1.36 cm [CI, -2.49 to -0.23 cm]) reduced pain at less than 2 hours.

Moderate-certainty evidence indicated that neither the combination of acetaminophen plus ibuprofen plus

Figure 1. Grading the certainty of evidence and strength of recommendations of ACP clinical guidelines using GRADE.

Grading Certainty of Evidence			
High	Confident that the true effect is close to the estimated effect.		
Moderate	Moderately confident in the effect estimate: The true effect is likely close to the estimated effect, but there is a sizeable possibility that it is substantially different.		
Low	Confidence in the effect estimate is limited: The true effect may be substantially different from the estimated effect.		
Grading Recommendations			
Strength	Balance of Benefits and Harms	Applicable Patient Population	Policy Implications
Strong	Confidence that benefits clearly outweigh risks and burden or vice versa.	Applies to most patients in most circumstances.	Only strong recommendations could be considered as quality indicators to guide the development of accountability, reporting, and payment programs.
Conditional	Benefits probably outweigh risks and burden, or vice versa, but there is appreciable uncertainty.	Applies to many patients but may differ depending on circumstances or patients' values and preferences.	Policymaking will require substantial debates and involvement of many stakeholders. Policies are also more likely to vary between regions. Quality indicators would have to focus on the fact that adequate deliberation about the management options has taken place.

oxycodone nor tramadol alone showed statistically significant pain reduction at less than 2 hours compared with placebo. Low-certainty evidence indicated that the following combination treatments did not show statistically significant pain reduction at less than 2 hours compared with placebo: acetaminophen plus ibuprofen and ibuprofen plus cyclobenzaprine.

Pain Relief at 1 to 7 Days

Evidence was gathered from 69 RCTs with 10 829 patients (2).

Nonpharmacologic Treatments. Moderate-certainty evidence showed that on a 10-cm VAS, specific acupressure decreased pain (WMD, -2.09 cm [CI, -2.85 to -1.33 cm]) and supervised rehabilitation increased pain at 1 to 7 days (WMD, 1.06 [CI, 0.74 to 1.38 cm]) compared with placebo. Low-certainty evidence showed that TENS (WMD, -1.18 cm [-2.09 to -0.28 cm]) reduced pain at 1 to 7 days compared with placebo. The following interventions did not show statistically significant pain reduction at 1 to 7 days compared with placebo: ultrasound therapy (moderate-certainty evidence) and nonspecific acupressure, exercise, and laser therapy (low-certainty evidence).

Pharmacologic Treatments. High-certainty evidence showed that on a 10-cm VAS, acetaminophen plus opioids reduced pain at 1 to 7 days (WMD, -1.71 cm [CI, -2.97 to -0.46 cm]). Moderate-certainty evidence showed that the following interventions reduced pain at 1 to 7 days compared with placebo: acetaminophen alone (WMD, -1.07 cm [CI, -1.89 to -0.24 cm]), oral NSAIDs (WMD, -0.99 cm [CI, -1.46 to -0.52 cm]), and topical NSAIDs (WMD, -1.08 cm [CI, -1.40 to -0.75 cm]). Low-certainty evidence showed that acetaminophen plus chlorzoxazone (WMD, -2.92 cm [CI, -5.41 to -0.43 cm]) also reduced pain at 1 to 7 days compared with placebo.

The following treatments did not show statistically significant pain reduction at 1 to 7 days compared with placebo: acetaminophen plus oral diclofenac, topical NSAIDs plus menthol gel, and glucosamine (moderate-certainty evidence) and ibuprofen plus cyclobenzaprine, acetaminophen plus ibuprofen, cyclobenzaprine, and menthol gel (low-certainty evidence).

Physical Function

Evidence was gathered from 31 RCTs with 3549 patients (2).

Nonpharmacologic Treatments. Moderate-certainty evidence showed that on a 10-cm VAS, specific acupressure improved physical function compared with placebo (WMD, 1.51 cm [CI, 1.23 to 1.80 cm]). Low-certainty evidence did not show a statistically significant improvement in function compared with placebo for nonspecific acupressure, joint manipulation, education, exercise, mobilization, TENS, or supervised rehabilitation.

Pharmacologic Treatments. Moderate-certainty evidence showed that on a 10-cm VAS, oral NSAIDs (WMD, 0.73 cm [CI, 0.17 to 1.30 cm]) and topical NSAIDs (WMD, 1.66 cm [CI, 1.16 to 2.16 cm]) improved physical function compared with placebo. Menthol gel (moderate-certainty evidence) and acetaminophen

(low-certainty evidence) did not show a statistically significant improvement in function compared with placebo.

Treatment Satisfaction

Evidence was gathered from 17 studies with 10 390 patients (2).

Nonpharmacologic Treatments. Low-certainty evidence showed that specific and nonspecific acupressure and mobilization did not improve treatment satisfaction compared with placebo.

Pharmacologic Treatments. High-certainty evidence showed that topical NSAIDs provided more treatment satisfaction than placebo (OR, 5.20 [CI, 2.03 to 13.33]). The following interventions did not improve treatment satisfaction compared with placebo: oral NSAIDs (moderate-certainty evidence), acetaminophen alone or plus oral diclofenac (moderate-certainty evidence), and ibuprofen plus cyclobenzaprine (low-certainty evidence).

Symptom Relief

Evidence was gathered from 26 RCTs with 4067 patients (2).

Nonpharmacologic Treatments. Moderate-certainty evidence showed that laser therapy improved symptom relief (OR, 32.08 [CI, 6.55 to 157.2]), and low-certainty evidence showed that mobilization improved symptom relief (OR, 7.99 [CI, 1.29 to 49.41]). Low-certainty evidence showed that specific and nonspecific acupressure, TENS, and education did not have a statistically significant effect on symptom relief.

Pharmacologic Treatments. High-certainty evidence showed that acetaminophen plus opioids (OR, 1.44 [CI, 1.03 to 2.03]) increased the likelihood of symptom relief compared with placebo. Moderate-certainty evidence showed that acetaminophen plus oral diclofenac (OR, 3.72 [CI, 1.02 to 13.52]), oral NSAIDs (OR, 3.10 [CI, 1.39 to 6.91]), and topical NSAIDs (OR, 6.39 [CI, 3.48 to 11.75]) also improved symptom relief. Low-certainty evidence showed an improvement in symptom relief with topical NSAIDs plus menthol gel (OR, 13.34 [CI, 3.30 to 53.92]). Acetaminophen alone or plus ibuprofen did not show a statistically significant improvement in symptom relief compared with placebo (moderate-certainty evidence).

Comparative Effectiveness of Nonpharmacologic and Pharmacologic Treatments

Interventions that had statistically significant benefit compared with placebo and at least 1 other intervention were considered to be "among the most effective" interventions. For pain reduction at less than 2 hours, moderate-certainty evidence showed that the following interventions were among the most effective: acetaminophen, acetaminophen plus oral diclofenac, oral NSAIDs, and topical NSAIDs alone or plus menthol. Low-certainty evidence showed that transbuccal fentanyl may be among the most effective for pain reduction at less than 2 hours. Moderate-certainty evidence showed that for pain reduction at 1 to 7 days, acetaminophen, oral NSAIDs, and topical NSAIDs may be among the most effective in-

interventions. Low-certainty evidence showed that acetaminophen plus chlorzoxazone, specific acupressure, and TENS may be among the most effective. Moderate-certainty evidence showed that topical NSAIDs were among the most effective interventions for improvement in function. Low-certainty evidence showed that specific acupressure may be among the most effective. High-certainty evidence showed that topical NSAIDs were among the most effective interventions for treatment satisfaction. Moderate-certainty evidence showed that acetaminophen plus oral diclofenac, oral NSAIDs, and topical NSAIDs were among the most effective interventions for symptom relief.

Harms of Nonpharmacologic and Pharmacologic Treatment

The systematic review pooled evidence from included RCTs on dermatologic, GI, and neurologic adverse events.

Dermatologic Adverse Events

Thirty-nine studies comprising 7235 patients reported dermatologic adverse events (2). The following specific adverse events were reported: application site or local reactions, burning or hot-cold sensation, dermatitis, dry skin, edema, erythema, inflammation, irritation, itching, lipothymia, pain, perspiration, pruritus, pyrexia, rash, and urticaria. Dermatologic adverse events did not differ significantly between any intervention and placebo.

GI Adverse Events

Forty-five studies comprising 7070 patients reported GI adverse events (2). The following specific adverse events were reported: abdominal pain or cramps, bleeding, constipation, diarrhea, distension, dry mouth, dyspepsia, epigastric pain or discomfort, flatulence, gastritis, gastroenteritis, heartburn, indigestion, nausea, salivation, ulcer, and vomiting. Moderate-certainty evidence showed that transbuccal fentanyl (OR, 59.38 [CI, 6.21 to 567.71]), acetaminophen plus opioids (OR, 5.63 [CI, 2.84 to 11.16]), and oral NSAIDs (OR, 1.77 [CI, 1.33 to 2.35]) increased risk for GI adverse events.

The following interventions did not show a statistically significant increase in GI adverse events compared with placebo: laser therapy, topical NSAIDs, and tramadol (moderate-certainty evidence) and specific and nonspecific acupressure, joint manipulation, mobilization, exercise, supervised rehabilitation, TENS, cyclobenzaprine, ibuprofen plus cyclobenzaprine, and acetaminophen alone or with chlorzoxazone (low-certainty evidence).

Neurologic Adverse Events

Thirty-eight studies comprising 6245 patients reported neurologic adverse events (2). The following specific adverse events were reported: agitation, anxiety, blurred vision, confusion, dizziness, drowsiness, dysphoria, fatigue, headache, insomnia, lightheadedness, malaise, nerve palsies, nervousness, paresthesia,

sedation, sleepiness, somnolence, tiredness, and vertigo. High-certainty evidence showed that acetaminophen plus opioids (OR, 3.53 [CI, 1.92 to 6.49]) increased neurologic adverse events more than placebo. Moderate-certainty evidence showed an increase in neurologic adverse events with tramadol (OR, 6.72 [CI, 1.24 to 36.39]) and transbuccal fentanyl (OR, 5.73 [CI, 1.20 to 27.47]), and low-certainty evidence showed an increase with ibuprofen plus cyclobenzaprine (OR, 4.91 [CI, 1.45 to 16.61]).

The following did not show a statistically significant increase in neurologic adverse events compared with placebo: oral NSAIDs, laser therapy, and phenylramidol (moderate-certainty evidence) and specific and non-specific acupressure, exercise, mobilization, joint manipulation, supervised rehabilitation, TENS, cyclobenzaprine, and topical NSAIDs (low-certainty evidence).

Comparative Harms of Nonpharmacologic and Pharmacologic Treatments

Interventions that showed statistically significant harm compared with placebo and at least 1 other intervention were considered to be “among the most harmful” interventions. For neurologic adverse events, acetaminophen plus opioids (high-certainty evidence) and tramadol alone (moderate-certainty evidence) were among the most harmful. For GI adverse events, acetaminophen plus opioids and transbuccal fentanyl alone were among the most harmful interventions (moderate-certainty evidence).

Opioid Use–Related Harms: Predictors of Prolonged Opioid Use

The evidence review team did a separate systematic review for predictors of prolonged opioid use after a prescription to treat acute musculoskeletal pain (13). The overall prevalence of prolonged opioid use for low-risk populations (that is, not receiving wage replacement benefits and having low representation of substance use disorder) was 6% (CI, 4% to 8%). Moderate-certainty evidence showed an association between prolonged opioid use and greater physical comorbidity (absolute risk increase [ARI], 0.9% [CI, 0.1% to 1.7%]), age (ARI for every 10-year increase, 1.1% [CI, 0.7% to 1.5%]), and past or present substance use disorder (ARI, 10.5% [4.2% to 19.8%]). Low-certainty evidence from studies that could not be pooled showed that prolonged opioid use was associated with prescriptions lasting more than 7 days (ARI ranged from 2% to 9%) and higher morphine milligram equivalents per day (ARI ranged from 2% to 13%).

VALUES AND PREFERENCES

We identified no systematic reviews on patient values and preferences for the management of acute pain from non-low back, musculoskeletal injury for any of the interventions included in the review. We surveyed the CGC Public Panel to collect preferences regarding the benefits and harms of these interventions. Five of 7 panel members responded to the survey (response rate, 71%). All 5 indicated that, on the basis of the reported clinical bene-

fits and harms, they would select topical NSAIDs or oral acetaminophen. Four of 5 members indicated that they would consider oral NSAIDs or specific acupressure, and 3 of 5 would consider TENS. No respondents indicated that they would select tramadol or transbuccal fentanyl. Public Panel members reported that they would not consider selecting opioids because the harms outweighed the benefits, and 1 member would not select oral NSAIDs because of the GI-related harms.

COSTS

The evidence-to-decision table (Supplement 1) reports the costs of nonpharmacologic and pharmacologic treatments, and we limited this information to interventions that showed a statistically significant difference for 1 or more outcomes.

INCONCLUSIVE AREAS OF EVIDENCE

Head-to-head comparisons to show superiority of one intervention over another were lacking (2).

MULTIPLE CHRONIC CONDITIONS: CLINICAL CONSIDERATIONS

Persons with more chronic conditions have a higher probability of receiving opioids for prolonged periods (13).

RECOMMENDATIONS

Figure 2 summarizes the recommendations and clinical considerations.

Recommendation 1: ACP and AAFP recommend that clinicians treat patients with acute pain from non-low back, musculoskeletal injuries with topical NSAIDs with or without menthol gel as first-line therapy to reduce or relieve symptoms, including pain; improve physical function; and improve the patient's treatment satisfaction (Grade: strong recommendation; moderate-certainty evidence).

Topical NSAIDs were the only intervention that improved all outcomes in patients with acute pain from non-low back, musculoskeletal injuries. They were among the most effective interventions for treatment satisfaction (high-certainty evidence) and for pain reduction at less than 2 hours and at 1 to 7 days; function; and symptom relief, which was generally defined as marked or full symptom resolution (moderate-certainty evidence). Furthermore, topical NSAIDs were not associated with a statistically significant increase in risk for adverse effects (low- to high-certainty evidence). Topical NSAIDs plus menthol gel also improved pain at less than 2 hours (moderate-certainty evidence) and symptom relief (low-certainty evidence). Although there is no evidence that the combination provides additional benefit over topical NSAIDs alone, harms are unlikely to increase, and offering the combination therapy as another treatment option is reasonable. Because heterogeneity in the presentation of acute pain is consider-

able, topical NSAIDs may not always be appropriate first-line therapy, such as in cases of severe injury.

Recommendation 2a: ACP and AAFP suggest that clinicians treat patients with acute pain from non-low back, musculoskeletal injuries with oral NSAIDs to reduce or relieve symptoms, including pain, and to improve physical function, or with oral acetaminophen to reduce pain (Grade: conditional recommendation; moderate-certainty evidence).

Recommendation 2b: ACP and AAFP suggest that clinicians treat patients with acute pain from non-low back, musculoskeletal injuries with specific acupressure to reduce pain and improve physical function, or with transcutaneous electrical nerve stimulation to reduce pain (Grade: conditional recommendation; low-certainty evidence).

Moderate-certainty evidence showed that oral NSAIDs reduced pain at less than 2 hours and at 1 to 7 days after treatment and were associated with a greater likelihood of symptom relief (generally defined as marked or complete symptom resolution) in patients with acute pain from non-low back, musculoskeletal injuries. There was also moderate-certainty evidence that acetaminophen reduced pain at less than 2 hours and at 1 to 7 days. Oral NSAIDs were associated with increased risk for GI adverse events (moderate-certainty evidence), including but not limited to GI bleeding, abdominal or stomach pain, constipation, diarrhea, dyspepsia, nausea, and vomiting. The costs of oral NSAIDs and acetaminophen did not differ substantially. Clinicians should assess patients' risk factors (GI and renal) and treatment preferences in choosing between oral NSAIDs and acetaminophen.

Specific acupressure improved pain at 1 to 7 days and function (moderate-certainty evidence), but only low-certainty evidence indicated that specific acupressure improved pain at less than 2 hours. Low-certainty evidence suggested that TENS improved pain at less than 2 hours and at 1 to 7 days. Of note, definitions of acupressure varied across trials and are summarized in the accompanying network meta-analysis (2). The CGC could not determine the cost of TENS or specific acupressure and therefore did not use cost considerations to recommend one over the other.

The CGC recommended only interventions that improved at least 2 outcomes, with the exception of acetaminophen plus oral diclofenac because the CGC judged that combination therapy offered no benefit over single therapy and because the harms noted for single-therapy oral NSAIDs would apply to this combination. Interventions that improved only 1 outcome were massage therapy (moderate-certainty evidence), acetaminophen plus ibuprofen plus codeine (low-certainty evidence), and transbuccal fentanyl (low-certainty evidence) for pain at less than 2 hours; acetaminophen plus chlorzoxazone and ibuprofen plus cyclobenzaprine for pain at 1 to 7 days after treatment (low-certainty evidence); and laser therapy for symptom relief (low-certainty evidence).

Recommendation 3: ACP and AAFP suggest against clinicians treating patients with acute pain from

Figure 2. Summary of the ACP and AAFP guideline on treatment of acute musculoskeletal pain in adults.

Nonpharmacologic and Pharmacologic Management of Acute, Non–Low Back, Musculoskeletal Pain in Adults

? Background

Musculoskeletal injuries are common and are most frequently treated in outpatient settings. Acute, non–low back, musculoskeletal pain lasts less than 4 weeks and includes strains and sprains, soft-tissue injuries, whiplash, and a variety of other conditions ranging from non surgical fractures to contusions. There are numerous treatment options, including nonpharmacologic and pharmacologic interventions (nonopioid and opioid). For the treatment of low back pain, please see [ACP's 2017 guideline on Noninvasive Treatments for Acute, Subacute, and Chronic Low Back Pain](#).



Patient Population

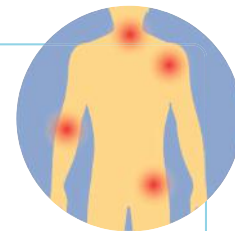
Adults with acute, non–low back, musculoskeletal pain



Interventions Compared

Any nonpharmacologic or pharmacologic therapy that could be delivered in the outpatient setting

Only interventions included in the final recommendations are summarized below. Please see guideline for complete list of interventions compared, including those that were not effective or had insufficient evidence.



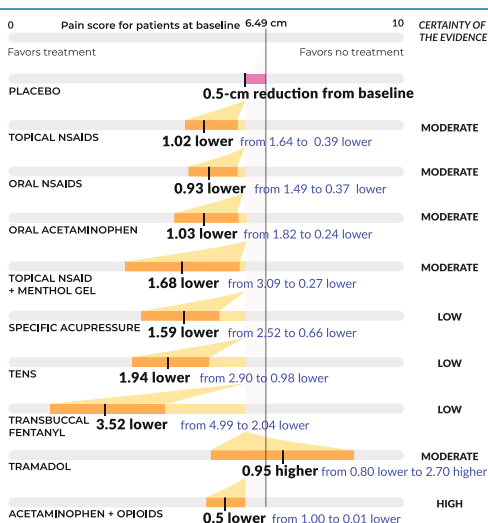
Outcomes Evaluated

Pain and physical function

Reported as changes in score on a 10-point scale. Results are the weighted mean difference (WMD) on scale of 0 to 10. A difference of 1 cm represents the smallest change that is considered important.

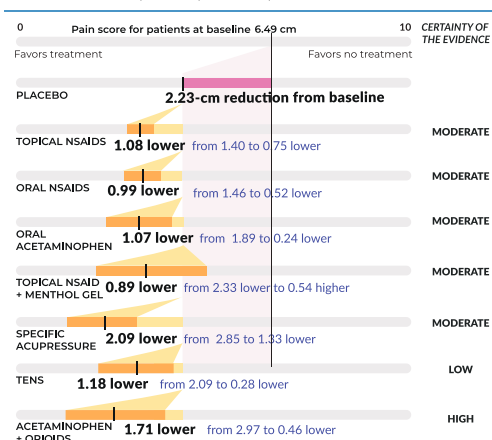
Pain reduction <2h

On a scale of 0 to 10 (higher scores signal higher pain), how much did the intervention reduce pain compared with placebo?



Pain reduction 1 to 7 days

On a scale of 0 to 10 (higher scores signal higher pain), how much did the intervention reduce pain compared with placebo?



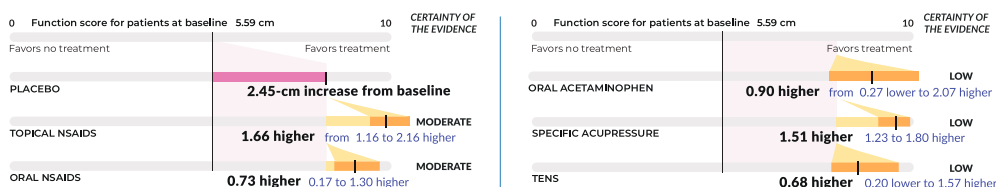
Data were not available for the following interventions: transbuccal fentanyl, tramadol

Continued on the following page

Figure 2–Continued.

Physical function improvement

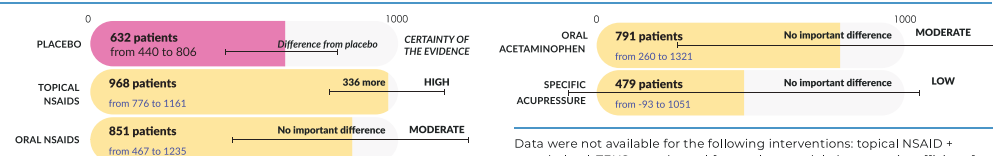
On a scale of 0 to 10 (higher scores signal better physical function), how much did the intervention improve function compared with placebo?



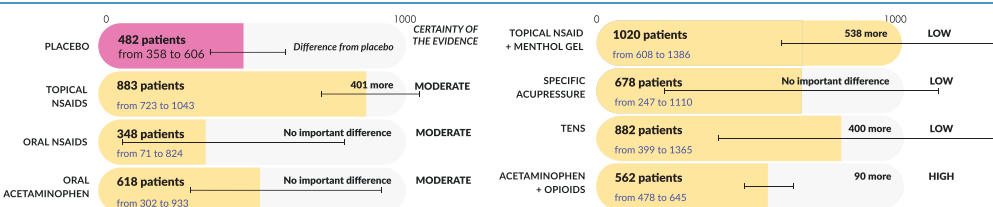
Data were not available for the following interventions: topical NSAID + menthol gel, transbuccal fentanyl, tramadol, and acetaminophen + opioid

Treatment satisfaction and symptom relief

How many events will be produced per 1000 patients treated?

Treatment satisfaction

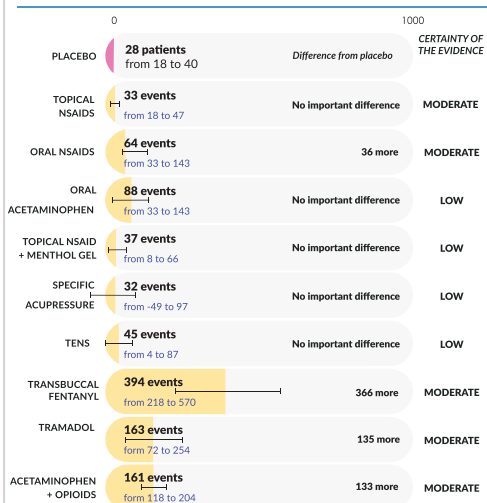
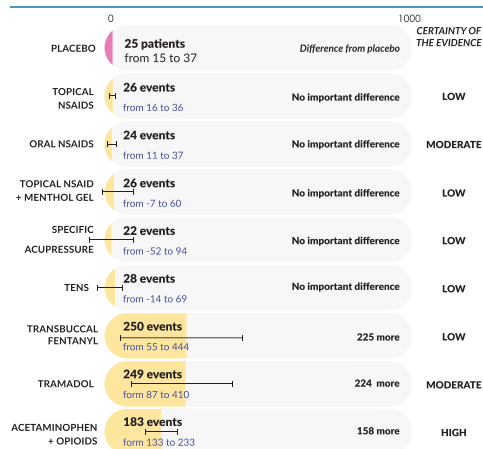
Data were not available for the following interventions: topical NSAID + menthol gel, TENS, transbuccal fentanyl, tramadol; data were insufficient for the following intervention: acetaminophen + opioids

Symptom relief

Data were not available for the following interventions: transbuccal fentanyl, tramadol

Adverse events

How many gastrointestinal and neurologic adverse events will be produced per 1000 patients treated? There were not important differences, or data were not available, for dermatologic adverse events.

GI-related AEs**Neurologic-related AEs**

Data were not available for the following interventions: oral acetaminophen

Figure 2–Continued.

Predictors of Prolonged Opioid Use

Low-certainty evidence showed that longer prescribing periods (>7 days compared with 1 to 3 days) and higher morphine milligram equivalents per day were predictors of risk for prolonged use.

Values and Preferences

Values and preferences vary according to individual patients. Clinicians and patients should select treatment options on the basis of a discussion of the benefits, harms, and costs of the interventions.

Recommendations

RECOMMENDATION 1: ACP and AAFP recommend that clinicians treat patients with acute pain from non–low back, musculoskeletal injuries with topical NSAIDs with or without menthol gel as first-line therapy to reduce or relieve symptoms, including pain; improve physical function; and improve the patient's treatment satisfaction (Grade: strong recommendation; moderate-certainty evidence).

RATIONALE: Topical NSAIDs were the only intervention that improved all outcomes compared with placebo in patients with acute pain from non–low back, musculoskeletal injuries. Topical NSAIDs were among the most effective interventions for beneficial outcomes and were not associated with increased risk for harms. Topical NSAIDs plus menthol gel also reduced or relieved symptoms, including pain; though there is no evidence that the combination provides added benefit over topical NSAIDs alone, it can be considered as another treatment option.

RECOMMENDATION 2a: ACP and AAFP suggest that clinicians treat patients with acute pain from non–low back, musculoskeletal injuries with oral NSAIDs to reduce or relieve symptoms, including pain, and to improve physical function, or with oral acetaminophen to reduce pain (Grade: conditional recommendation; moderate-certainty evidence).

RECOMMENDATION 2b: ACP and AAFP suggest that clinicians treat patients with acute pain from non–low back, musculoskeletal injuries with specific acupressure to reduce pain and improve physical function, or with transcutaneous electrical nerve stimulation to reduce pain (Grade: conditional recommendation; low-certainty evidence).

RATIONALE: Evidence showed that these interventions improved at least 2 of the following outcomes: pain at ≤2 hours' duration, pain at 1 to 7 days after treatment, function, and symptom relief. There were few reported harms, except for oral NSAIDs, which are associated with gastrointestinal adverse events. Clinicians should assess gastrointestinal risk factors before prescribing oral NSAIDs and should prescribe the lowest effective dose for the shortest period necessary.

RECOMMENDATION 3: ACP and AAFP suggest against clinicians treating patients with acute pain from non–low back, musculoskeletal injuries with opioids, including tramadol (Grade: conditional recommendation; low-certainty evidence).

RATIONALE: Opioid interventions were associated with large increases in the risk for neurologic and GI adverse events. Evidence showed a relationship between prescriptions lasting longer than 7 days and prolonged use of opioids, and opioids are associated with longer-term addiction and overdose.

Clinical Considerations

- Clinicians should inform patients with acute, non–low back, musculoskeletal pain that topical NSAIDs have favorable outcomes and fewer side effects than oral medications. Studies looked only at topical diclofenac, and the results may not translate for compounded formulations.
- Insurers should make prescription topical NSAIDs accessible for the management of acute, non–low back, musculoskeletal pain because they improve a number of outcomes and have fewer harms than other medications. However, topical NSAIDs are often not available without prior authorization.
- Clinicians should avoid prescribing therapies with substantial potential harms, such as opioids. Tramadol is a narcotic and, like other opioids, is associated with the risk for prolonged use and abuse. Even in cases of severe injury, consider restricting duration of opioid prescription to ≤ 7 days.
- Oral NSAIDs are associated with increased risk for GI bleeding, and NSAID-associated GI bleeding risk is higher in the elderly than in the nonelderly. Also, the risk for renal dysfunction associated with oral NSAID use is higher in the elderly, particularly among persons concurrently taking angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers. Oral NSAIDs can worsen blood pressure control among persons with hypertension. Clinicians should consider the baseline age of the patient, pre existing hypertension, and history of GI bleeding before prescribing oral NSAIDs.
- Treatment characteristics (dosages, duration, administration) varied across studies.

Talking Points for Patients

- Topical NSAIDs work better than oral medications and are less likely to cause harm. Oral NSAIDs, such as ibuprofen work better than acetaminophen but have a risk for potential kidney and gastrointestinal side effects.
- Opioids or transbuccal fentanyl are not recommended except in cases of severe injury because they are not more effective than other pain medications and can cause serious harms, such as dependency and even death.



non-low back, musculoskeletal injuries with opioids, including tramadol (Grade: conditional recommendation; low-certainty evidence).

High-certainty evidence showed that acetaminophen plus opioids reduced pain at 1 to 7 days and improved symptom relief; it also reduced pain at less than 2 hours, but this effect was small and not clinically important. On the other hand, none of the other 4 opioid interventions (transbuccal fentanyl, tramadol, and acetaminophen plus ibuprofen plus codeine or oxycodone) were associated with improvements in more than 1 outcome. Moreover, moderate- to high-certainty evidence indicated that opioid interventions were associated with large increases in risk for neurologic and GI adverse effects.

Evidence from observational studies also indicated that a substantial proportion of patients who are prescribed opioids for acute pain continue using prescription opioids over the long term (27% among high-risk populations and 6% among the general population). Low-certainty evidence showed that longer prescribing periods (>7 days vs. 1 to 3 days) and higher morphine milligram equivalents per day were predictors of risk for prolonged use. The Public Panel and nonphysician CGC members indicated that they would not select any of the opioids because the harms outweigh the benefits. Combination therapies with opioids also cost more than similar interventions without opioids, and many effective nonopioid alternatives exist for the management of acute pain. Therefore, except in cases of severe injury or intolerance of first-line therapies, clinicians should avoid prescribing these therapies because they are associated with substantial potential harms with little or no benefit and are associated with longer-term addiction and overdose.

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Note: Clinical practice guidelines are “guides” only and may not apply to all patients and all clinical situations. Thus, they are not intended to override clinicians’ judgment. All ACP clinical practice guidelines are considered automatically withdrawn or invalid 5 years after publication, or once an update has been issued.

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References

1. United States Bone and Joint Initiative. The burden of musculoskeletal diseases in the United States. 3rd ed. 2014. Accessed at www.boneandjointburden.org on 1 July 2019.
2. Busse JW, Sadeghirad B, Oparin Y, et al. Management of acute pain from non-low back musculoskeletal injuries. A systematic review and network meta-analysis of randomized trials. *Ann Intern Med*. 18 August 2020. [Epub ahead of print]. doi:10.7326/M19-3601
3. Chou R, Deyo R, Friedly J, et al. Systemic pharmacologic therapies for low back pain: a systematic review for an American College of Physicians clinical practice guideline. *Ann Intern Med*. 2017;166:480-492. [PMID: 28192790] doi:10.7326/M16-2458
4. Chou R, Deyo R, Friedly J, et al. Nonpharmacologic therapies for low back pain: a systematic review for an American College of Physicians clinical practice guideline. *Ann Intern Med*. 2017;166:493-505. [PMID: 28192793] doi:10.7326/M16-2459
5. Hsu JR, Mir H, Wally MK, et al. Clinical practice guidelines for pain management in acute musculoskeletal injury. *J Orthop Trauma*. 2019;33:e158-e182. [PMID: 30681429]
6. Qaseem A, Wilt TJ, McLean RM, et al. Noninvasive treatments for acute, subacute, and chronic low back pain: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2017;166:514-530. [PMID: 28192789] doi:10.7326/M16-2367
7. Daubresse M, Chang HY, Yu Y, et al. Ambulatory diagnosis and treatment of nonmalignant pain in the United States, 2000-2010. *Med Care*. 2013;51:870-8. [PMID: 24025657]
8. Delgado MK, Huang Y, Meisel Z, et al. National variation in opioid prescribing and risk of prolonged use for opioid-naïve patients treated in the emergency department for ankle sprains. *Ann Emerg Med*. 2018;72:389-400.e1. [PMID: 30054152]
9. Finney FT, Gossett TD, Hu HM, et al. Rate of opioid prescriptions for patients with acute ankle sprain. *Ann Intern Med*. 2019;171:441-443. [PMID: 31284299] doi:10.7326/M19-0679
10. Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use. National Academies Pr; 2017.
11. Qaseem A, Kansagara D, Lin JS, et al. The development of clinical guidelines and guidance statements by the Clinical Guidelines Committee of the American College of Physicians: update of methods. *Ann Intern Med*. 2019;170:863-870. [PMID: 31181568] doi:10.7326/M18-3290
12. Qaseem A, Wilt TJ, et al. Disclosure of interests and management of conflicts of interest in clinical guidelines and guidance statements: methods from the Clinical Guidelines Committee of the American College of Physicians. *Ann Intern Med*. 2019;171:354-361. [PMID: 31426089] doi:10.7326/M18-3279
13. Riva JJ, Noor ST, Wang L, et al. Predictors of prolonged opioid use after initial prescription for acute musculoskeletal injuries in adults. A systematic review and meta-analysis of observational studies. *Ann Intern Med*. 18 August 2020. [Epub ahead of print]. doi:10.7326/M19-3600
14. Schünemann H, Brożek J, Guyatt G, et al, eds. GRADE Handbook. Updated October 2013. Accessed at <http://gdt.guideline-development.org/app/handbook/handbook.html> on 2 July 2019.

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APPENDIX: DETAILED METHODS

A team at McMaster University conducted the supporting evidence review. Details of the ACP guideline development process can be found in ACP's methods paper (11). Disclosure of interests and management of any conflicts can be found at www.acponline.org/clinical_information/guidelines/guidelines/conflicts_cgic.htm.

Key Questions Addressed

The accompanying systematic evidence review and network meta-analysis (2) addressed the following key question: In adult patients with acute (<4 weeks), non-low back, musculoskeletal pain in the outpatient setting, what are the effectiveness and comparative effectiveness (benefits and harms, both short-term and long-term) of nonpharmacologic treatments, nonopioid pharmacologic treatments, and opioid treatments?

An additional review (13) also addressed the following question: What factors are associated with prolonged opioid use after prescription to treat acute musculoskeletal pain in adults?

Search Strategy

Reviewers searched several databases (MEDLINE, Embase, CINAHL, PEDro, and CENTRAL) for studies and systematic reviews published from inception through February 2018.

Quality Assessment

Reviewers assessed risk of bias as described in the evidence reviews (2, 13).

Population Studied

The population studied was adults with acute pain from non-low back, musculoskeletal injuries.

Interventions Evaluated

Interventions included both pharmacologic and nonpharmacologic treatments for acute pain from non-low back, musculoskeletal injuries.

Comparators

Interventions were compared versus placebo and versus each other.

Outcomes

Outcomes were pain (at 15 minutes to 2 hours, 1 to 7 days, and 3 weeks to 6 months); function; symptom relief; patient satisfaction; and GI, dermatologic, and neurologic adverse events.

Target Audience

The target audience is all clinicians.

Target Patient Population

The target patient population is adults with acute pain from non-low back, musculoskeletal injuries.

Public and Patient Involvement

The development of this guideline also included perspectives, values, and preferences of 2 nonphysician CGC members who represent the public and a 7-member CGC Public Panel.

Peer Review

The supporting evidence review and guideline each underwent a peer review process through the journal. The guideline was posted online for comments from ACP Regents and ACP Governors, who represent internal medicine and its subspecialty physician members at the national and international levels. It was also reviewed by members of AAFP's Commission on Health of the Public and Science.