# Systematic Review on Treatments for Acute Pain: Surveillance Report 2

**Literature Update Period: November 1, 2021, through January 22, 2022**

## Background and Purpose

This is the second surveillance report for the 2020 report *Treatments for Acute Pain: A Systematic Review (https://effectivehealthcare.ahrq.gov/products/treatments-acute-pain/research)*,[1] covering the period November 1, 2021, through January 22, 2022. The 2020 report addressed benefits and harms of opioid, nonopioid pharmacologic, and nonpharmacologic treatments for specific types of acute pain (low back pain, neck pain, other musculoskeletal pain, neuropathic pain, postoperative pain [excluding inpatient management of pain after major surgical procedures], dental pain, pain due to kidney stones, and pain due to sickle cell disease). Given the clinical and public health importance of this topic, it is important to identify new evidence that could impact practice or policy. The purpose of this update is to identify new evidence published since the last surveillance report, published in October 2021 (Surveillance Report 1), and to determine how the new evidence impacts the findings of the original 2020 report and Surveillance Report 1. A subsequent update is planned for May 2022 (based on evidence published through April 2022).

## Scope

The scope and eligibility criteria established at the time of the original report[1] were utilized for this surveillance report; no changes were made. The report addressed the following acute pain conditions:

- Acute back pain (including back pain with radiculopathy) (Key Question [KQ] 1)
- Acute neck pain (including neck pain with radiculopathy) (KQ 2)
- Musculoskeletal pain not otherwise included in KQ 1 or KQ 2 (including fractures) (KQ 3)
- Peripheral neuropathic pain (related to herpes zoster and trigeminal neuralgia) (KQ 4)
- Postoperative pain (excluding inpatient management of pain following major surgical procedures) (KQ 5)
- Dental pain (KQ 6)
- Kidney stones (including inpatient management) (KQ 7)
- Sickle cell crisis (episodic pain) (KQ 8)

For each of these acute pain conditions, the report addressed the effectiveness and comparative effectiveness (benefits and harms) for the following comparisons:

- Opioid therapy versus nonopioid pharmacologic therapy (acetaminophen, non-steroidal anti-inflammatory drugs [NSAIDs], skeletal muscle relaxants, benzodiazepines, antidepressants, anticonvulsants, cannabis) or nonpharmacologic therapy (exercise,

cognitive behavioral therapy, meditation, relaxation, music therapy, virtual reality, acupuncture, massage, manipulation/mobilization, physical modalities).
- Nonopioid pharmacologic therapy versus other nonopioid pharmacologic treatments or nonpharmacologic therapy.
- Nonpharmacologic therapy versus inactive treatments or usual care.

The report also addressed how benefits and harms varied according to demographic, clinical, and medication factors; effects on short- and long-term opioid use of prescribing opioid therapy for acute pain conditions; and factors influencing opioid prescribing for acute pain conditions. The full protocol for the original report, including detailed inclusion criteria using the PICOTS (populations, interventions, comparisons, outcomes, timing, settings) framework (https://www.ncbi.nlm.nih.gov/books/NBK566503/table/appb.tab1/?report=objectonly) and full KQs (https://www.ncbi.nlm.nih.gov/books/NBK566501/#ch3.s2), is shown in the appendixes and is also available on the Agency for Healthcare Research and Quality website (https://effectivehealthcare.ahrq.gov/products/treatments-acute-pain/protocol) and on the PROSPERO systematic reviews registry (CRD42020165677).

## Methods

Update searches were conducted to identify evidence published from November 2020 through January 22, 2022. Search strategies from the original report were utilized[1] and we searched the same databases as in the original report (Ovid® MEDLINE®, PsycINFO®, Embase®, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews). In addition, to capture articles not yet indexed in MEDLINE, we supplemented the original search strategies with an optimized (text-word only) search[2] in pre-MEDLINE to identify studies not yet indexed with Medical Subject Headings (MeSH). As in the original report, searches on electronic databases were for English-language studies and supplemented by review of reference lists of relevant articles. Search strategies are shown in Appendix A. Randomized controlled trials were included for all KQs. Controlled observational studies (cohort, case-control, and before-after studies) were also included for opioid prescribing and effects on long-term use, accuracy and effectiveness of risk prediction instruments, and factors influencing prescribing.

As in the original review, one investigator screened all citations identified through searches for eligibility for full-text review. (KQs and inclusion criteria are available in Appendix B.) In addition, to increase efficiency of abstract review, we utilized the artificial intelligence function in Distiller SR (DistillerSR AI) in conjunction with a second investigator to assist in conducting dual review. DistillerSR AI utilizes Natural Language Processing to train itself and make inclusion predictions using manually reviewed references. DistillerSR AI was trained using 2,132 abstracts identified in the searches conducted for Surveillance Report 1. All citations from the searches conducted for this update were manually reviewed by one investigator. The trained DistillerSR AI assigned a certainty score for each citation, indicating how likely it was to qualify for inclusion (from 0.0 to 1.0 probability of inclusion); a second investigator performed dual review on all studies assigned a DistillerSR AI certainty score of 0.40 or more. Any citation identified as potentially eligible by either reviewer underwent full-text review to determine final eligibility.

We utilized the same methods for data abstraction and quality assessment as the original report. We assessed the quality of individual controlled trials using the approach recommended

in the chapter Assessing the Risk of Bias of Individual Studies When Comparing Medical Interventions in the *Methods Guide for Effectiveness and Comparative Effectiveness Reviews,* developed by the Agency for Healthcare Research and Quality,[3] in conjunction with criteria and methods developed by the Cochrane Back Review Group.[4] We excluded combination treatments except for an opioid plus NSAIDs or acetaminophen, as these combinations are commonly used in clinical practice and frequently evaluated in clinical trials. When possible, we stratified comparisons according to whether an opioid was administered alone or in combination with an NSAID or acetaminophen. We separately evaluated single dose trials and multidose trials (i.e., trials that evaluated a course of more than one dose of therapy).

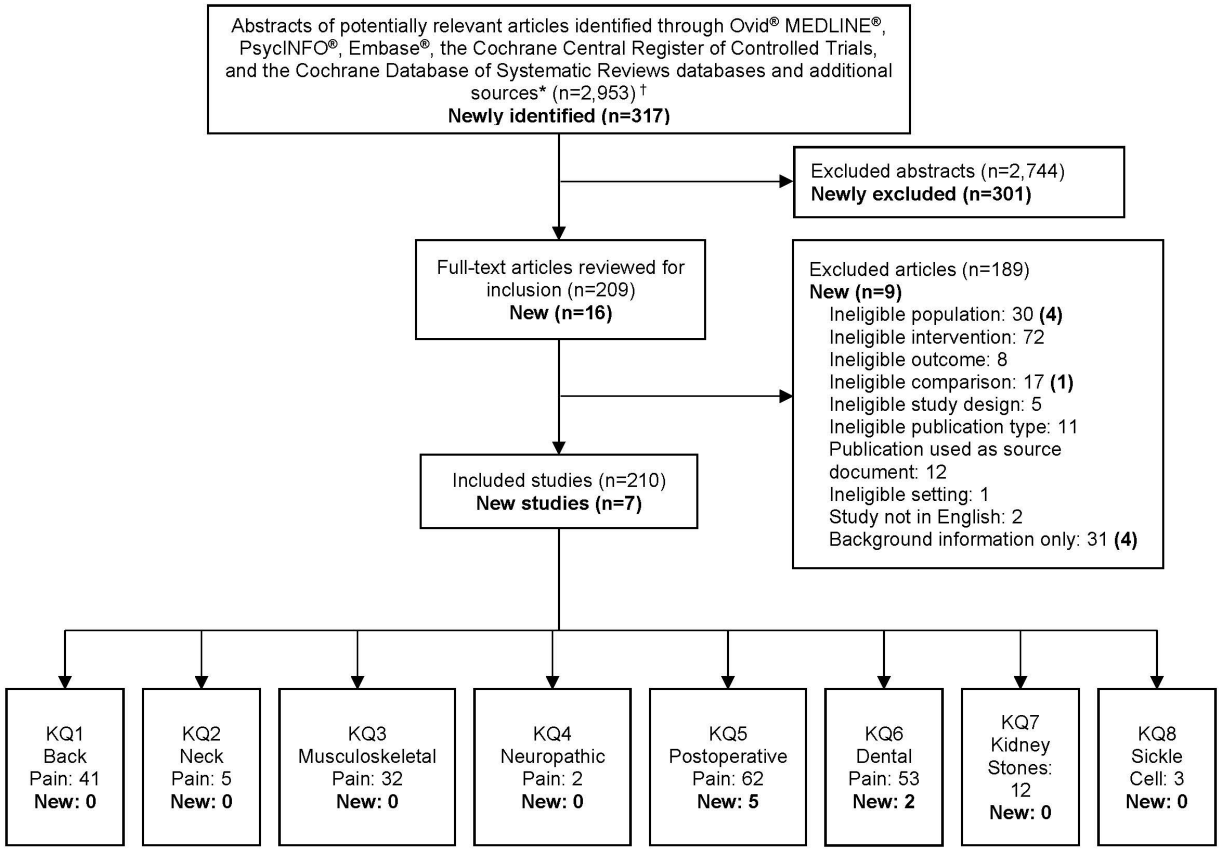
The decision to update meta-analyses from the original report was based on the number and sample sizes of new studies eligible for meta-analysis (meta-analysis performed if new evidence was large relative to the studies in the original meta-analysis); consistency in findings between the new studies and the original meta-analysis (meta-analysis performed if findings from new evidence appear inconsistent and new studies were appropriate for pooling based on similarity in populations, interventions, and comparisons, in order to determine whether new studies impact conclusions); or whether new evidence could impact the strength of evidence (SOE) (meta-analysis performed if the SOE based on the original meta-analysis was low or insufficient and new evidence could increase the SOE due to increased precision, high quality, or other factors). The SOE was based on the totality of evidence (evidence in the original report plus new evidence) and determined using the methods described in the original report. Changes in the SOE assessments resulting from this current surveillance update are described separately from the findings reported in Surveillance Report 1.

A list of included studies identified for this update is provided in Appendix C and a list of articles excluded at full text, along with reasons for exclusion, is available in Appendix D. Evidence tables providing data from included studies are available in Appendix E, quality assessments for each study are shown in Appendix F, and forest plots for updated meta-analyses are shown in Appendix G.

# Results

The search for Surveillance Report 2 from November 1, 2021, to January 22, 2022, yielded 317 citations, and identified 7 new eligible trials (5 randomized controlled trials[5-9] and 2 pseudo-randomized [by birth year] trials[10,11]) (Figure 1). Five trials[6,7,9-11] addressed acute (non-dental) postoperative pain and two[5,8] addressed acute post-surgical dental pain. Of the acute (non-dental) postoperative pain trials, one[6] evaluated an abdominal binder (no prior trials) and one[7] evaluated transcutaneous electrical nerve stimulation (TENS; 1 prior trial); three trials[9-11] evaluated preoperative education and effects on opioid prescribing (no prior trials). Both trials of acute post-surgical dental pain evaluated opioids plus acetaminophen or an NSAID versus an NSAID (single dose [1 new trial;[5] 12 prior trials] or a multidose course of therapy [1 new trial;[8] 3 prior trials]). No new eligible studies were identified for acute low back pain, neck pain, musculoskeletal pain, peripheral neuropathic pain, kidney stone pain, or sickle cell pain, or effects of opioid use versus non-use for specific pain conditions and likelihood of short- or long-term use. Two trials (both evaluating patients with acute postoperative dental pain) were rated good quality,[5,8] 2 trials were rated fair quality,[7,9] and 3 trials were rated poor quality (Appendix F).[6,10,11] Methodological limitations in the poor-quality trials included lack of randomization (allocation by birth year), open-label design, and high attrition without intention-to-treat analysis.

**Figure 1. Literature flow diagram**




Abbreviations: KQ = Key Question
*Additional sources include prior reports, reference lists of relevant articles, systematic reviews, etc.
†Search counts are for the surveillance report searches only. Included studies totals are from the original report and surveillance reports combined. ("New" indicates newly included in Surveillance Report 2.)

# Summary of Findings

- Seven new trials were identified for this update (5 postoperative pain and 2 dental pain). Four of the five new trials evaluated interventions for acute postoperative pain without prior evidence (1 trial of an abdominal binder and 3 trials on effects of preoperative education on opioid prescribing). Both new trials of patients with acute postoperative dental pain evaluated previously assessed drug comparisons (single dose or multidose course of therapy of opioid plus NSAID or acetaminophen versus NSAID).

## KQ1: Acute Back Pain

- No new evidence was found.

## KQ 2: Acute Neck Pain

- No new evidence was found.

## KQ3: Musculoskeletal Pain Not Included in KQ1 or KQ2

- No new evidence was found.

## KQ4: Peripheral Neuropathic Pain

- No new evidence was found.

## KQ5: Postoperative Pain

- One new poor-quality trial was insufficient to determine effects of an abdominal binder. No prior trial evaluated abdominal binders or braces for acute postoperative pain.
- One new trial found TENS associated with a small decrease in pain intensity versus sham TENS at day 2; these findings were consistent with the original report.
- Three new trials found preoperative education associated with decreased opioid use at 1 to 2 weeks versus no education, with no increase in pain intensity. No prior trials evaluated effects of preoperative education on opioid use.

## KQ6: Dental Pain

- One new trial found a multidose course of an opioid plus acetaminophen or NSAID associated with small non–statistically significant decrease in pain intensity versus an NSAID at less than 1 day; there were no differences in pain intensity at 24 and 48 hours and no differences in likelihood of a positive global assessment. These findings were judged to be consistent with the original report and Surveillance Report 1.
- One new trial found a *single dose* of an opioid plus NSAID associated with moderate increase in pain intensity versus an NSAID at less than 1 day; these findings were consistent with the original report and Surveillance Report 1.
- Two new trials found opioid-containing regimens were associated with increased likelihood of harms versus an NSAID alone, including any adverse event, nausea, vomiting, dizziness, and drowsiness; these findings were consistent with the original report.
- One new trial found no difference in pain intensity between a *multidose* course of an opioid plus acetaminophen versus acetaminophen in patients with acute nonoperative dental pain at less than 1 day or 1 day to less than 1 week, and no difference in rescue analgesic use. This finding was consistent with one small trial included in the original report.
- One new trial found a single dose of an opioid plus acetaminophen associated with small to moderate decrease in pain intensity versus acetaminophen at 4 to 48 hours in patients with acute nonoperative dental pain; statistical significance was not reported, and the new trial was too small to resolve the inconsistency reported for this comparison and outcome in the original report.
- Two new trials found an opioid plus acetaminophen associated with increased likelihood of drowsiness, dizziness, nausea, and vomiting versus acetaminophen; these findings were consistent with the original report.
- One new trial found an NSAID associated with a small decrease in pain intensity at less than 1 day versus acetaminophen; these findings were consistent with the original report.

## KQ7: Kidney Stones

- No new evidence was found.

## KQ8: Sickle Cell Crisis

- No new evidence was found.

# Summary of New Evidence

Table 1 provides the conclusions from the 2020 report and the findings from studies identified in the surveillance reports. Table 1 focuses on KQs and comparisons/outcomes with any new evidence from the surveillance. Key Questions with new evidence identified in Surveillance Report 2 are shaded. The entire strength of evidence (SOE) table from the original 2020 review is available at https://www.ncbi.nlm.nih.gov/books/NBK566513/.

New evidence identified for Surveillance Report 2 included two new SOE ratings where none existed before: an abdominal binder was associated with a small decrease in pain versus no binder at 1 day to less than 1 week (SOE: insufficient), and preoperative education was associated with decreased opioid use at 1 to 2 weeks versus no preoperative education (SOE: low). With the addition of one new trial from Surveillance Report 2, the SOE rating for small to moderate decrease in pain at 1 day to less than 1 week with TENS versus sham TENS was upgraded from low to moderate.

**Table 1. Summary of conclusions and assessments informed by evidence from surveillance reports**

| Key Question | Conclusions From 2020 Report | Findings From Surveillance Reports 1 and 2 | Updated Conclusions Following Surveillance Reports |
|---|---|---|---|
| **1 (Low back pain): Traditional Chinese acupuncture vs. sham or usual care** | **Pain at 2 to <4 weeks: decreased** (SOE: low, based on 1 RCT) with acupuncture vs. non-penetrating sham or usual care but not needle sham | 1 RCT (n=167) found no difference between traditional Chinese acupuncture vs. usual care in pain, functional status, or quality of life at 2 to 4 weeks. | SOE downgraded to insufficient due to inconsistency |
| **3 (Musculoskeletal pain): Opioid plus acetaminophen vs. acetaminophen** | No evidence. | One RCT (n=154) found an opioid associated with small decrease in pain but increased likelihood of adverse events and drowsiness. | SOE: Low for pain and adverse events |
| **3 (Musculoskeletal pain): Topical ibuprofen vs. capsaicin** | No evidence. | One RCT (n=119) inconclusive due to poor quality. | SOE: Insufficient |
| **5 (Postoperative pain): Opioid vs. NSAID, multidose** | **Pain, 1 day to <1 week: Inconsistent findings** (SOE: insufficient, based on 4 RCTs).<br><br>**Rescue medication use, 1 day to <1 week:** RR 1.22 to 2.04 (SOE: moderate, based on 4 RCTs) | One RCT (n=70) found opioid associated with a small increase in pain at day 1, with no difference at day 7. | Unchanged |

| Key Question | Conclusions From 2020 Report | Findings From Surveillance Reports 1 and 2 | Updated Conclusions Following Surveillance Reports |
|---|---|---|---|
| **5 (Postoperative pain): Opioid vs. acetaminophen, multidose** | **Evidence limited and inconsistent for pain and other outcomes**; each RCT evaluated outcomes at a different time point (<1 day, 1 day to <1 week, and 2 to <4 weeks) (SOE: insufficient, based on 3 RCTs) | One RCT (n=80) found no difference between an opioid vs. acetaminophen in pain at day 7. | Unchanged |
| **5 (Postoperative pain): Opioid vs. mixed agent** | **Pain: No difference** at <1 day (1 RCT, SOE: low), 1 day to <1 week (6 RCTs, SOE: moderate), or 1 to <2 weeks (1 RCT, SOE: low) | One RCT (n=91) found no difference between an opioid vs. tapentadol in pain at 1 day to <1 week, 1 to <2 weeks, or ≥4 weeks. | SOE unchanged at <1 day and at 1 day to <1 week, upgraded to moderate for 1 to <2 weeks, and assessed as low for ≥4 weeks |
| **5 (Postoperative pain): Cold therapy vs. sham or no cold therapy** | **Pain, <1 week: No difference** (SOE: low, based on 3 RCTs)<br><br>**Pain, function, QoL, 2 to <4 weeks and ≥4 weeks: No differences** (SOE: low, based on 1 RCT) | One RCT (n=100) found continuous cooling for 7 days associated with moderate decrease in pain versus usual care at 1 day to <1 week, with no differences at 1 to <2 weeks or ≥4 weeks in pain intensity, function, or QoL; two RCTs (n=100 and 137) reported inconsistent results for a cold pack vs. usual care in pain intensity at <1 day to 1 day. | SOE unchanged for cold therapy vs. sham therapy (no new RCTs)<br><br>SOE insufficient (based on 2 RCTs) for cold therapy vs. usual care and pain intensity at <1 day due to inconsistency; low (based on 1 RCT) for moderate benefit at 1 day to <1 week; and low for no difference at 1 to <2 weeks and ≥4 weeks |
| **5 (Postoperative pain): Music therapy vs. no music therapy** | **Pain, <1 day and 1 day to <1 week: Small to moderate decrease** (SOE: low, based on 2 RCTs) | One RCT (n=47) found music therapy associated with a small decrease in pain intensity on day 1 that was not statistically significant; the difference was moderate and statistically significant on day 4. | SOE at 1 day to <1 week upgraded to moderate |
| **5 (Postoperative pain): Abdominal binder vs. no binder** | No evidence | ***New for Surveillance Report 2:*** One RCT (n=196)[6] found an abdominal binder associated with small decrease in pain vs. no binder at 1 day to <1 week, but had serious methodological limitations. | ***New SOE (no prior evidence): Insufficient (based on 1 new RCT)**** |
| **5 (Postoperative pain): TENS vs. sham TENS** | **Pain, <1 day and 1 day to <1 week: Small to moderate decrease** (SOE: low, based on 1 RCT) | ***New for Surveillance Report 2:*** One RCT (n=80)[7] found TENS associated with a small decrease in pain intensity vs. sham TENS at 1 day to <1 week. | ***SOE at 1 day to <1 week upgraded to moderate**** |
| **5 (Postoperative pain): Preoperative education vs. no education** | No evidence | ***New for Surveillance Report 2:*** Three RCTs (n=445)[9,10,11] found preoperative education associated with decreased opioid use at 1 to 2 weeks vs. no preoperative education, with similar or decreased pain intensity. | ***New SOE for opioid use (no prior evidence): Low (based on 3 new RCTs)**** |

| Key Question | Conclusions From 2020 Report | Findings From Surveillance Reports 1 and 2 | Updated Conclusions Following Surveillance Reports |
|---|---|---|---|
| **6 (Dental pain): Opioid plus acetaminophen or NSAID vs. NSAID, multidose** | **Pain, <1 day and 1 day to <1 week: No difference** (SOE: low, based on 1 RCT [<1 day] and 3 RCTs [1 day to 1 week])<br><br>**Global improvement: No difference** (SOE: low, based on 2 RCTs) | One RCT (n=620) found similar effects of a multidose course of an opioid plus NSAID vs. an NSAID on pain intensity at 6 and 24 hours and increased likelihood of a positive global assessment.<br><br>***New for Surveillance Report 2*:** One RCT (n=70)[8] found an opioid plus NSAID versus NSAID associated with a small, non-statistically significant decrease in pain intensity at <1 day, with no difference at 1 day to 1 week. There was no difference in likelihood of a positive global assessment. | Unchanged (an updated meta-analysis for likelihood of positive global assessment again found no difference) |
| **6 (Dental pain): Opioid vs. NSAID, multidose** | **Pain, <1 day and 1 day to <1 week: No difference** (SOE: insufficient, based on 1 RCT) | One RCT (n=412) found similar effects of a multidose course of an opioid alone vs. NSAID on pain intensity and likelihood of a positive global assessment in patients with postoperative dental pain. | SOE upgraded to low |
| **6 (Dental pain): Opioid plus acetaminophen or NSAID vs. NSAID, single dose** | **Pain, <1 day and 1 day to <1 week: Small to moderate increase at <1 day and no difference at 1 day to <1 week** (SOE: low, based on 12 RCTs [<1 day] and 3 RCTs [1 day to <1 week]) | One RCT (n=60) found a single dose of an opioid plus acetaminophen associated with a small to moderate decrease in pain intensity versus an NSAID at <1 day and at 1 day to <1 week, but did not report statistical significance of findings.<br><br>***New for Surveillance Report 2:*** One RCT (n=169)[5] found a single dose of an opioid plus acetaminophen associated with moderate increase in pain intensity versus an NSAID at <1 day, but did not report statistical significance of findings. | Unchanged |
| **6 (Dental pain): Opioid (with or without acetaminophen or NSAID) vs. NSAID** | **Opioid increased risk of: Any adverse event**: RR 1.72 (95% CI 1.29 to 2.28) **Nausea:** RR 2.72 (95% CI 1.84 to 4.01) **Dizziness:** RR 2.97 (95% CI 1.59 to 5.54) **Drowsiness:** RR 1.76 (95% CI 1.00 to 3.10) (SOE: moderate, based on 9 to 12 RCTs) | Two RCTs (n=825 and 60) found opioids associated with increased risk of any adverse event, nausea, dizziness, and drowsiness.<br><br>***New for Surveillance Report 2:*** Two RCTs (n=80 and 177)[5,8] found opioids associated with increased risk of any adverse event, nausea, and dizziness. | Unchanged |

| Key Question | Conclusions From 2020 Report | Findings From Surveillance Reports 1 and 2 | Updated Conclusions Following Surveillance Reports |
|---|---|---|---|
| **6 (Dental pain): Opioid plus acetaminophen vs. acetaminophen, multidose course** | **Pain, <1 day:** One very small (n=20) RCT found opioid associated with large improvement (SOE: insufficient) | One RCT (n=39) found no differences in pain or rescue analgesic use among patients with nonoperative dental pain. | Unchanged (remained insufficient due to imprecision and inconsistency) |
| **6 (Dental pain): Opioid plus acetaminophen vs. acetaminophen, single dose** | **Pain, <1 day: Inconsistent effect** (SOE: moderate, based on 11 RCTs)<br><br>**Rescue or repeat medication use, <1 day: RR 0.81 (95% CI 0.56 to 0.97)** (SOE: moderate, based on 7 RCTs) | One RCT (n=60) found an opioid associated with moderate to large decrease in pain intensity versus the NSAID at <1 day and 1 day to <1 week, although statistical significance was not reported. | Unchanged |
| **6 (Dental pain): Opioid plus acetaminophen vs. acetaminophen** | **Opioids increased risk of:**<br>**Any adverse event**: RR 1.43 (95% CI 0.87 to 2.37)<br>**Nausea:** RR 1.55 (95% CI 0.75 to 3.18)<br>**Drowsiness:** RR 2.03 (95% CI 0.70 to 5.93)<br>**Dizziness:** RR 2.49 (95% CI 0.66 to 9.49)<br>(SOE: low, based on 4 to 8 RCTs) | Two RCTs (n=39 and 60) found opioids associated with increased risk of any adverse events (2 RCTs, 26.6% vs. 0% and 35% vs. 16%), dizziness (1 RCT, 15% vs. 5%), nauseas (1 RCT, 40% vs. 11%), and vomiting (1 RCT, 10% vs. 0%). | Unchanged |
| **6 (Dental pain): NSAID vs. acetaminophen** | **Pain intensity, rescue or repeat medication use: Moderate to large decrease**<br>**Rescue or repeat medication use: decrease** (RR 0.64, 95% CI 0.58 to 0.71) (SOE: moderate, based on 11 to 15 RCTs) | One RCT (n=60) found an NSAID associated with small decrease in pain at <1 day (p-value not reported). | Unchanged |

*SOE assessments impacted by new evidence identified for surveillance Report 2
Abbreviations: CI = confidence interval; NSAID = nonsteroidal anti-inflammatory drug; QoL = quality of life; RCT = randomized controlled trial; RR = relative risk; SOE = strength of evidence; TENS = transcutaneous electrical nerve stimulation.

# Evidence Details

## Key Question 1: Acute Back Pain

We did not identify any new trials evaluating interventions for acute back pain.

## Key Question 2: Acute Neck Pain

We did not identify any new trials evaluating interventions for acute neck pain.

## Key Question 3: Musculoskeletal Pain Not in KQ1 or KQ2

We did not identify any new trials evaluating interventions for acute musculoskeletal pain.

## Key Question 4: Peripheral Neuropathic Pain

We did not identify any new trials evaluating interventions for peripheral neuropathic pain.

## Key Question 5: Postoperative Pain

### Abdominal Binder Versus No Binder

The original report included no trials of an abdominal binder or brace for acute postoperative pain. One new poor-quality trial (n=196) evaluated an abdominal binder following cesarean section versus no binder.[6] There was no difference in pain intensity at 24 hours (2.5 vs. 2.75 on 0 to 10 scale, p value not reported); at 48 hours, the binder was associated with a small decrease in pain intensity (2.25 vs. 3.22, p=0.002). There was also no difference in opioid use.

### TENS Versus Sham TENS

The original report included one trial that found TENS associated with moderate to large decrease in pain intensity versus sham TENS following liposuction at less than 1 day and at 1 day to less than 1 week (SOE: low). TENS was also associated with decreased analgesic use; no serious adverse events were reported.

One new fair-quality trial (n=80) compared TENS versus sham TENS following inguinal surgery. TENS was associated with decreased pain intensity versus sham TENS, with differences that ranged from 0.47 to 0.79 on a 0 to 10 visual analog scale (VAS) for pain relief at rest, on walking, or on standing.[7] No adverse events were reported.

### Preoperative Education Versus No Education

The original report included no trials on effects of preoperative education on postoperative opioid use. Three new trials (one fair quality[9] and two poor quality[10,11]) evaluated preoperative education in patients undergoing outpatient orthopedic or thyroid/parathyroid surgery. Preoperative education included information on the opioid epidemic, risks of opioids, safe use of opioids, and use of nonopioid therapies. In one trial, patients who received preoperative education received opioids only if requested ("opt-in"); the other trials did not apply specific parameters regarding opioid use.

Preoperative education was consistently associated with decreased opioid use at 1 to 2 weeks following surgery, without an increase in pain intensity. In one fair-quality trial, preoperative education with opt-in opioid use was associated with decreased number of opioid tablets dispensed versus no preoperative education (mean 4.8 vs. 10.1, p<0.001).[9] Preoperative education and opt-in opioid use was also associated with decreased morphine equivalents consumed, although the difference was not statistically significant (median 15 vs. 20 mg, p=0.49). There were no differences in pain intensity or quality of life. Two poor-quality trials also found preoperative education (not requiring patients to opt in to opioid use) associated with decreased opioid use versus no preoperative education (mean morphine equivalents 45.0 vs. 83.8 mg, p=0.01 and 46.4 vs. 92.7, p=0.02).[10,11] Preoperative education was associated with moderate to large decrease in pain intensity at 1 day to less than 1 week versus no education in one trial and no difference in pain intensity in the other.

## Key Question 6: Dental Pain

### Opioid Versus NSAID

The original report found a single dose of an opioid plus acetaminophen or NSAID associated with small to moderate increase in pain intensity versus an NSAID at less than 1 day (12 trials), increased likelihood of rescue or repeat medication use (9 trials, relative risk [RR]

1.35, 95% confidence interval [CI] 1.23 to 1.48), and decreased likelihood of global improvement (5 trials, RR 0.64, 95% CI 0.53 to 0.76) (SOE: low for pain intensity and global improvement, moderate for rescue or repeat medication use). There was no difference between a multidose course of therapy with an opioid plus acetaminophen or an NSAID versus an NSAID alone in pain intensity at 1 day to less than 1 week (3 trials) or likelihood of global improvement (2 trials, RR 1.15, 95% CI 0.52 to 2.57) (SOE: low). Opioids were associated with increased likelihood of any adverse event (11 trials, pooled RR 1.72, 95% CI 1.29 to 2.28), nausea (12 trials, pooled RR 2.72, 95% CI 1.84 to 4.01), dizziness (10 trials, pooled RR 2.97, 95% CI 1.59 to 5.54), and drowsiness (9 trials, pooled RR 1.76, 95% CI 1.00 to 3.10) versus an NSAID alone (SOE: moderate). Most trials in the original report evaluated patients with acute postoperative dental pain (most commonly, third molar extraction). In the original report, meta-analysis was not performed for mean pain intensity because results at specific time points were estimated in most trials from figures, and standard deviations were not reported; sums of pain intensity differences were not pooled because methods of calculation varied (pain scales utilized and number and timing of assessments).

Surveillance Report 1 added two trials of an opioid plus acetaminophen or NSAID versus NSAID for acute dental pain.[12,13] One trial of patients with acute non-surgical dental pain found a single dose of an opioid plus acetaminophen associated with a small to moderate decrease in pain intensity versus an NSAID in patients with acute non-surgical dental pain at 4 to 48 hours (statistical significance not reported).[13] Despite some inconsistency with the trials in the original report, the new trial did not change the SOE ratings for single dose opioid plus NSAID or acetaminophen versus NSAIDs, given its small size relative to the trials in the original report. The second trial,[12] which evaluated a multidose course of therapy in patients undergoing third molar extraction, reported results consistent with the original report with regard to pain intensity; an updated meta-analysis also reported similar results for global improvement.

Two new trials of an opioid plus acetaminophen or NSAID versus an NSAID for acute dental pain were identified for Surveillance Report 2.[5,8] One new trial (n=169) compared a single dose of an opioid (hydrocodone 10 mg) plus acetaminophen (650 mg) versus naproxen sodium 440 mg following third molar extraction.[5] The opioid plus acetaminophen was associated with a small increase in pain intensity versus the NSAID at 12 hours, based on less improvement in pain intensity (mean change from baseline -2.2 vs. -4.0 on a 0 to 10 numeric rating scale, p value not reported). The trial did not report likelihood of global improvement or likelihood of rescue or repeat medication use.

The second new trial (n=70) compared tramadol 75 mg plus dexketoprofen 25 mg versus ibuprofen 400 mg every 8 hours for up to 48 hours following third molar extraction.[8] The opioid was associated with a small reduction in pain intensity at 12 hours that was not statistically significant (2.42 vs. 3.26 on a 0 to 10 VAS, p=0.09). At 48 hours, results slightly favored the NSAID, although the difference was below the threshold for small (0.37 point) and not statistically significant (p=0.81). There was no difference in the likelihood of global improvement (80.6% vs. 73.5%, RR 1.10, 95% CI 0.85 to 1.42). An updated meta-analysis with the new trial again showed no difference in the likelihood of global improvement (9 trials, N=1,041, RR 0.85, 95% CI 0.65 to 1.11, $I^2$=87%, **Appendix G**).

As in prior trials, the new trials found opioids were associated with increased risk of any adverse event (39.1% vs. 14.4% and 52.7% vs. 8.8%), nausea (34.5% vs. 1.1% and 19.4% vs. 0%), vomiting (21.8% vs. 0% and 8.3% vs. 0%), and dizziness (6.9% vs. 0% and 25.0% vs. 0%)

versus NSAIDs. The new trials found no differences in the proportion of patients with headache (1.1% vs. 0%) or somnolence (0% vs. 1.1% and 8.3% vs. 2.9%).

### Key Question 7: Kidney Stones (Including Inpatient Management)

We did not identify any new trials evaluating interventions for kidney stone pain.

### Key Question 8: Sickle Cell Crisis (Episodic Pain)

We did not identify any new trials evaluating interventions for pain associated with acute sickle cell crises.

## Conclusions

The original report and Surveillance Report 1 evaluated opioid therapy, nonopioid pharmacologic therapies, and nonpharmacologic therapies for selected acute pain conditions. Opioid therapy was associated with decreased or similar effectiveness for pain versus an NSAID for surgical dental pain, kidney stone pain, and low back pain. Opioids and NSAIDs were more effective than acetaminophen for surgical dental pain and acute musculoskeletal pain, but opioids were less effective than acetaminophen for kidney stone pain. Opioids were associated with increased risk of short-term adverse events versus NSAIDs or acetaminophen, including any adverse event, nausea, dizziness, and somnolence. Serious adverse events were uncommon for all interventions, but studies were not designed to assess risk of overdose, opioid use disorder, or long-term harms. Being prescribed an opioid for acute low back pain or postoperative pain was associated with increased likelihood of use of opioids at long-term followup versus not being prescribed, based on observational studies, although potential confounding could have impacted findings. Evidence on nonpharmacologic therapies was limited, but heat therapy, spinal manipulation, massage, acupuncture, acupressure, a cervical collar, music therapy, TENS, and exercise were effective for specific acute pain conditions. Evidence was limited on the comparative effectiveness of therapies for sickle cell pain, acute neuropathic pain, neck pain, and management of postoperative pain following discharge; effects of therapies for acute pain on non-pain outcomes; effects of therapies on long-term outcomes, including long-term opioid use; and how benefits and harms of therapies vary in subgroups.

For Surveillance Report 2, new evidence was found only for postoperative pain and acute postsurgical dental pain. One new trial was consistent with prior evidence in finding TENS associated with decreased pain intensity versus sham TENS. Although one new trial evaluated an abdominal binder for postoperative pain, it had serious methodological limitations and was insufficient to determine effects. A new finding from this surveillance report is that preoperative education is associated with decreased opioid use with similar or reduced pain intensity versus no preoperative education (no prior trials). For acute postsurgical dental pain, two new trials of an opioid plus NSAID or acetaminophen versus NSAID were consistent with prior evidence. As previously noted, more evidence is needed to determine whether effects of pharmacologic therapy differ for acute post-surgical and nonoperative dental pain. New studies were found only for postoperative pain and dental pain; therefore, previously described gaps for sickle cell pain, acute neuropathic pain, and neck pain remain. No new studies were identified on the association between opioid use versus non-use for specific acute pain conditions and short- or long-term opioid use.

The next surveillance report is scheduled for May 2022.

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# Acknowledgments

The authors gratefully acknowledge the following individuals for their contributions to this project: research associate Christina Bougatsos, M.P.H., and student research assistant Keeley Black, B.S., both from Oregon Health & Science University; and Task Order Officer Suchitra Iyer, Ph.D., at the Agency for Healthcare Research and Quality.

# Disclaimers

This report is based on research conducted by the Pacific Northwest Evidence-based Practice Center under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 75Q80120D00005). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help healthcare decision makers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.



AHRQ or U.S. Department of Health and Human Services endorsement of any derivative products that may be developed from this report, such as clinical practice guidelines, other quality enhancement tools, or reimbursement or coverage policies, may not be stated or implied.

AHRQ appreciates appropriate acknowledgment and citation of its work. Suggested language for acknowledgment: This work is the second update report of a living systematic review, Treatments for Acute Pain: A Systematic Review, by the Evidence-based Practice Center Program at the Agency for Healthcare Research and Quality (AHRQ).

**Suggested citation:** Chou R, Griffin JC, Blazina I, Schwarz E, Atchison C, Mauer K. Systematic Review on Treatments for Acute Pain: Surveillance Report 2. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 75Q80120D00005.) AHRQ Publication No. 22-EHC022. Rockville, MD: Agency for Healthcare Research and Quality; March 2022.
DOI: https://doi.org/10.23970/AHRQEPCSURVEILLANCE2ACUTEPAIN. Posted final reports are located on the Effective Health Care Program search page.

# Afterword

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of healthcare in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new healthcare technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see https://effectivehealthcare.ahrq.gov/about/epc/evidence-synthesis.

This and future quarterly progress reports will provide up-to-date information about the evidence base to inform health plans, providers, purchasers, government programs, and the healthcare system as a whole on the state of the science. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the website (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input.

If you have comments on this report, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov. They will be considered in the next version of the report.


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# Appendixes

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# Appendix A. Literature Search Strategies

**Ovid MEDLINE(R), All 1946 to January 22, 2022**

1. Pain/
2. Acute Pain/
3. Pain Management/
4. (acute adj3 pain).ti,ab,kf.
5. exp back pain/ or exp musculoskeletal pain/ or neck pain/ or exp neuralgia/ or exp Facial Pain/ or exp Nephrolithiasis/ or exp Anemia, Sickle Cell/ or Pain, Postoperative/
6. (back or spine or spinal or radicular or neck or musculoskeletal or fracture* or neuropathic or neuralgia or neuropathy or sciatica or "dental pain" or "ondotogenic pain" or "kidney stone*" or urolithiasis or nephrolithiasis or "sickle cell" or "postoperative pain").ti,ab,kf.
7. treatment outcome/
8. exp Therapeutics/
9. (dh or dt or pc or rh or th).fs.
10. (treatment or therap* or intervention*).ti,ab,kf.
11. (or/1-4) and (5 or 6) and (or/7-10)
12. exp cohort studies/
13. cohort$.tw.
14. controlled clinical trial.pt.
15. epidemiologic methods/
16. limit 15 to yr=1966-1989
17. exp case-control studies/
18. (case$ and control$).tw.
19. or/12-14,16-18
20. randomized controlled trial.pt.
21. (random* or placebo* or control* or trial or blind*).ti,ab.
22. (animals not humans).sh.
23. (comment or editorial or meta-analysis or practice-guideline or review or letter).pt.
24. (20 or 21) not (22 or 23)
25. review.pt.
26. (medline or medlars or embase or pubmed or cochrane).tw,sh.
27. (scisearch or psychinfo or psycinfo).tw,sh.
28. (psychlit or psyclit).tw,sh.
29. cinahl.tw,sh.
30. ((hand adj2 search$) or (manual$ adj2 search$)).tw,sh.
31. (electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.
32. (pooling or pooled or mantel haenszel).tw,sh.
33. (peto or dersimonian or der simonian or fixed effect).tw,sh.
34. or/26-33
35. 25 and 34
36. meta-analysis.pt.

37. meta-analysis.sh.
38. (meta-analys$ or meta analys$ or metaanalys$).tw,sh.
39. (systematic$ adj5 review$).tw,sh.
40. (systematic$ adj5 overview$).tw,sh.
41. (quantitativ$ adj5 review$).tw,sh.
42. (quantitativ$ adj5 overview$).tw,sh.
43. (quantitativ$ adj5 synthesis$).tw,sh.
44. (methodologic$ adj5 review$).tw,sh.
45. (methodologic$ adj5 overview$).tw,sh.
46. (integrative research review$ or research integration).tw.
47. or/36-46
48. 35 or 47
49. 19 or 24 or 48
50. 11 and 49
51. or/7-10
52. or/1-4
53. 51 and 52
54. (ultrasound or TENS or cold or cryotherapy).tw.
55. 53 and 54
56. ankle.tw.
57. 55 and 56
58. 57 not 50
59. limit 58 to english language
60. 49 and 59
61. musculoskeletal.tw.
62. 55 and 61
63. limit 62 to english language
64. 50 or 63
65. 60 or 64
66. (animal* or mouse or mice or rat* or dog* or canine or cow* or bovine or horse* or mare* or pig* or porcine or rabbit* or llama* or sheep or ewe*).ti.
67. 65 not 66
68. (202008$ or 202009$ or 20201$ or "2020 08 $" or "2020 09 $" or "2020 1$" or "2020 aug $" or "2020 sep $" or "2020 oct $" or "2020 nov $" or "2020 dec $").dp.
69. 67 and 68
70. limit 67 to yr="2021 -Current"
71. 69 or 70

**Ovid MEDLINE(R), All 1946 to January 22, 2022**

Key Question: Post operation pain supplemental search

1. treatment outcome/
2. exp Therapeutics/

3. (dh or dt or pc or rh or th).fs.
4. (treatment or therap* or intervention*).ti,ab,kf.
5. Pain, Postoperative/
6. "postoperative pain".ti,ab,kf.
7. 5 or 6
8. or/1-4
9. 7 and 8
10. (opioid* or hydrocodone or oxycodone or hydromorphone or fentanyl or buprenorphine or naltrexone or naloxone or tramadol or tapentadol).tw.
11. (acetaminophen or "nonsteroidal anti-inflammatory" or NSAID* or "skeletal muscle relaxant*" or SMR* or benzodiazepine* or antidepressant* or anticonvulsant* or cannabis or cannabinoid*).tw.
12. (exercise or "cognitive behavioral therapy" or CBT or meditation or relaxation or music or "virtual reality" or acupuncture or acupressure or electroacupuncture or massage or manipulation or mobilization or mobilisation or "physical modalit*" or "transcutaneous electrical nerve stimulation" or TENS or ultrasound or brace* or traction or heat or cold or cryo*).tw.
13. or/10-12
14. 9 and 13
15. and (random* or control* or placebo or sham or trial).ti,ab,kf.
16. randomized controlled trial.pt.
17. (random* or placebo* or control* or trial or blind*).ti,ab.
18. (animals not humans).sh.
19. (comment or editorial or meta-analysis or practice-guideline or review or letter).pt.
20. (16 or 17) not (18 or 19)
21. 14 and 20
22. 15 or 21
23. (pediatric* or preschool* or toddler* or infan* or child*).ti,ab.
24. 22 not 23
25. limit 24 to english language
26. (202008$ or 202009$ or 20201$ or "2020 08 $" or "2020 09 $" or "2020 1$" or "2020 aug $" or "2020 sep $" or "2020 oct $" or "2020 nov $" or "2020 dec $").dp.
27. 25 and 26
28. limit 25 to yr="2021 -Current"
29. 27 or 28

**EBM Reviews - Cochrane Central Register of Controlled Trials, January 2022**

1. Pain/
2. Acute Pain/
3. Pain Management/
4. (acute adj3 pain).ti,ab.

5. exp back pain/ or exp musculoskeletal pain/ or neck pain/ or exp neuralgia/ or exp Facial Pain/ or exp Nephrolithiasis/ or exp Anemia, Sickle Cell/ or Pain, Postoperative/
6. (back or spine or spinal or radicular or neck or musculoskeletal or fracture* or neuropathic or neuralgia or neuropathy or sciatica or "dental pain" or "ondotogenic pain" or "kidney stone*" or urolithiasis or nephrolithiasis or "sickle cell" or "postoperative pain").ti,ab.
7. treatment outcome/
8. exp Therapeutics/
9. (dh or dt or pc or rh or th).fs.
10. (treatment or therap* or intervention*).ti,ab.
11. (or/1-4) and (5 or 6) and (or/7-10)
12. limit 11 to medline records
13. 11 not 12
14. conference abstract.pt.
15. "journal: conference abstract".pt.
16. "journal: conference review".pt.
17. or/14-16
18. 13 not 17
19. limit 18 to yr="2020 -Current"

**EBM Reviews - Cochrane Database of Systematic Reviews, 2005 to January 22, 2022**

1. (back or spine or spinal or radicular or neck or musculoskeletal or fracture* or neuropathic or neuralgia or neuropathy or sciatica or "dental pain" or "ondotogenic pain" or "kidney stone*" or urolithiasis or nephrolithiasis or "sickle cell" or "postoperative pain").ti.
2. (treatment or therap* or intervention*).ti,ab.
3. 1 and 2
4. limit 3 to full systematic reviews
5. 4 not chronic.ti.
6. 5 not children.ti.
7. 5 not 6
8. 7 and adult*.ti.
9. 6 or 8 (300)
10. ("2020" or "2021").so.
11. 9 and 10

**Elsevier Embase, January 2022**

('backache'/exp OR 'musculoskeletal pain'/exp OR 'neuropathic pain'/exp OR 'neuralgia'/exp OR 'tooth pain'/exp OR 'postoperative pain'/exp OR (('sickle cell anemia'/exp OR 'sickle cell crisis'/exp) AND ('pain'/exp OR pain:ti,ab,kw))) AND 'drug therapy'/exp AND ('article'/it OR 'review'/it) AND 'human'/de AND ('cohort analysis'/de OR 'comparative study'/de OR 'controlled study'/de OR 'meta analysis'/de OR 'randomized controlled trial'/de OR 'randomized controlled

trial (topic)'/de OR 'systematic review'/de) AND [english]/lim AND [embase]/lim NOT ([embase]/lim AND [medline]/lim)

**PsycINFO, 1806 to January Week 2, 2021**

1. exp Pain/
2. chronic pain/
3. 1 not 2
4. sickle cell disease/
5. exp Back Pain/
6. exp neuralgia/ or exp peripheral neuropathy/
7. Pain Management/
8. pain.ti,ab.
9. (back or spine or spinal or radicular or neck or musculoskeletal or fracture* or neuropathic or neuralgia or neuropathy or sciatica or dental or ondotogenic or kidney or urolithiasis or nephrolithiasis or "sickle cell" or postoperative).ti,ab.
10. (7 or 8) and 9
11. (acute adj3 pain).ti,ab.
12. 3 or 4 or 5 or 6 or 10 or 11
13. exp treatment outcomes/
14. treatment effectiveness evaluation/
15. 12 and (13 or 14)
16. exp clinical trials/
17. (random* or control* or placebo or sham or trial or blind*).ti,ab.
18. 15 and (16 or 17)
19. limit 18 to english language
20. limit 19 to human
21. limit 20 to (childhood <birth to 12 years> or adolescence <13 to 17 years>)
22. 20 not 21
23. 22 not chronic.ti.
24. limit 23 to yr="2020 -Current"

**Ovid MEDLINE(R) ALL, 1946 to January 22, 2022**

*Acute Pain Risk*

1. Pain/
2. Acute Pain/
3. Pain Management/
4. (acute adj3 pain).ti,ab,kf.
5. exp back pain/ or exp musculoskeletal pain/ or neck pain/ or exp neuralgia/ or exp Facial Pain/ or exp Nephrolithiasis/ or exp Anemia, Sickle Cell/ or Pain, Postoperative/

6. (back or spine or spinal or radicular or neck or musculoskeletal or fracture* or neuropathic or neuralgia or neuropathy or sciatica or "dental pain" or "ondotogenic pain" or "kidney stone*" or urolithiasis or nephrolithiasis or "sickle cell" or "postoperative pain").ti,ab,kf.
7. (or/1-4) and (5 or 6)
8. exp Analgesics, Opioid/
9. opioid*.ti,ab,kw.
10. (buprenorphine or codeine or fentanyl or hydrocodone or hydromorphone or methadone or morphine or oxycodone or oxymorphone or tapentadol or tramadol).ti,ab,kw,sh,hw.
11. or/8-10
12. exp Opioid-Related Disorders/
13. (opioid adj2 (abuse or addict* or misuse or diversion)).ti,ab,kf.
14. 12 or 13
15. 7 and (11 or 14)
16. Decision Support Techniques/
17. "Predictive Value of Tests"/
18. Prognosis/
19. Risk Assessment/
20. Risk Factors/
21. Proportional Hazards Models/
22. "Reproducibility of Results"/
23. "Sensitivity and Specificity"/
24. (sensitivity or specificity or accuracy).ti,ab,kf.
25. (risk and (predict$ or assess$)).ti,ab,kf.
26. or/16-25
27. Patient Compliance/
28. Health Services Misuse/
29. Substance Abuse Detection/
30. Drug Monitoring/
31. (urine adj7 (screen$ or test$ or detect$)).ti,ab,kf.
32. Contracts/
33. Patient Education as Topic/
34. Drug Overdose/
35. or/27-34
36. risk$.ti,ab,kf.
37. ("risk evaluation and mitigation" or "rems").ti,ab,kf.
38. Risk Reduction Behavior/ or Risk/
39. or/36-38
40. 26 or 35 or 39
41. 15 and 40
42. limit 41 to english language
43. (202008$ or 202009$ or 20201$ or "2020 08 $" or "2020 09 $" or "2020 1$" or "2020 aug $" or "2020 sep $" or "2020 oct $" or "2020 nov $" or "2020 dec $").dp.
44. 42 and 43

45. limit 42 to yr="2021 -Current"
46. 44 or 45

**EBM Reviews - Cochrane Central Register of Controlled Trials, January 2022**

*Acute Pain Risk*

1. Pain/
2. Acute Pain/
3. Pain Management/
4. (acute adj3 pain).ti,ab.
5. exp back pain/ or exp musculoskeletal pain/ or neck pain/ or exp neuralgia/ or exp Facial Pain/ or exp Nephrolithiasis/ or exp Anemia, Sickle Cell/ or Pain, Postoperative/
6. (back or spine or spinal or radicular or neck or musculoskeletal or fracture* or neuropathic or neuralgia or neuropathy or sciatica or "dental pain" or "ondotogenic pain" or "kidney stone*" or urolithiasis or nephrolithiasis or "sickle cell" or "postoperative pain").ti,ab.
7. (or/1-4) and (5 or 6)
8. exp Analgesics, Opioid/
9. opioid*.ti,ab,kw.
10. (buprenorphine or codeine or fentanyl or hydrocodone or hydromorphone or methadone or morphine or oxycodone or oxymorphone or tapentadol or tramadol).ti,ab,kw,sh,hw.
11. or/8-10
12. exp Opioid-Related Disorders/
13. (opioid adj2 (abuse or addict* or misuse or diversion)).ti,ab.
14. 12 or 13
15. 7 and (11 or 14)
16. Decision Support Techniques/
17. "Predictive Value of Tests"/
18. Prognosis/
19. Risk Assessment/
20. Risk Factors/
21. Proportional Hazards Models/
22. "Reproducibility of Results"/
23. "Sensitivity and Specificity"/
24. (sensitivity or specificity or accuracy).ti,ab.
25. (risk and (predict$ or assess$)).ti,ab.
26. or/16-25
27. Patient Compliance/
28. Health Services Misuse/
29. Substance Abuse Detection/
30. Drug Monitoring/
31. (urine adj7 (screen$ or test$ or detect$)).ti,ab.
32. Contracts/
33. Patient Education as Topic/

34. Drug Overdose/
35. or/27-34
36. risk$.ti,ab.
37. ("risk evaluation and mitigation" or "rems").ti,ab.
38. Risk Reduction Behavior/ or Risk/
39. or/36-38
40. 26 or 35 or 39
41. 15 and 40
42. limit 41 to english language
43. limit 42 to yr="2020 -Current"

**Optimized PreMEDLINE Search:**
**Ovid MEDLINE(R) In-Process & In-Data-Review Citations, 1946 to January 22, 2022**

1. (acute adj3 pain).ti,ab.
2. (((back or spine or spinal or radicular or neck or musculoskeletal or fracture*) adj3 pain) or neuropathic or neuralgia or neuropathy or sciatica or "dental pain" or "ondotogenic pain" or "kidney stone*" or urolithiasis or nephrolithiasis or "sickle cell" or "postoperative pain").ti.
3. (treatment or therap* or intervention*).ti,ab.
4. (random* or placebo* or control* or trial or blind*).ti,ab.
5. (1 or 2) and 3
6. 4 and 5
7. (202008$ or 202009$ or 20201$ or "2020 08 $" or "2020 09 $" or "2020 1$" or "2020 aug $" or "2020 sep $" or "2020 oct $" or "2020 nov $" or "2020 dec $").dp.
8. 6 and 7
9. limit 6 to yr="2021 -Current"
10. 8 or 9
11. limit 10 to english language
12. chronic.ti.
13. 11 not 12

# Appendix B. Key Questions and Inclusion and Exclusion Criteria

## Key Questions

Each Key Question (KQ) for this review focuses on a specific acute pain condition. The conditions and related subquestions are listed below:

KQ1: Acute back pain (including back pain with radiculopathy)

KQ2: Acute neck pain (including neck pain with radiculopathy)

KQ3: Musculoskeletal pain not otherwise included in KQ1 or KQ2 (including fractures)

KQ4: Peripheral neuropathic pain (related to herpes zoster and trigeminal neuralgia)

KQ5: Postoperative pain (excluding inpatient management of pain following major surgical procedures)

KQ6: Dental pain (surgical and nonsurgical)

KQ7: Kidney stones (including inpatient management)

KQ8: Sickle cell crisis (episodic pain)

For each condition above, we addressed the following subquestions:

## Opioid Therapy

a. What is the comparative effectiveness of opioid therapy versus: (1) nonopioid pharmacologic therapy (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs], antidepressants, anticonvulsants) or (2) nonpharmacologic therapy (e.g., exercise, cognitive behavioral therapy, acupuncture) for outcomes related to pain, function, pain relief satisfaction, and quality of life and after followup at the following intervals: less than 1 day; 1 day to less than 1 week; 1 week to less than 2 weeks; 2 weeks to less than 4 weeks; 4 weeks or longer?

b. How does effectiveness of opioid therapy vary depending on: (1) patient demographics (e.g., age, race, ethnicity, gender); (2) patient medical or psychiatric comorbidities; (3) dose of opioids; (4) duration of opioid therapy, including number of opioid prescription refills and quantity of pills used; (5) opioid use history; (6) substance use history; (7) use of concomitant therapies?

c. What are the harms of opioid therapy versus nonopioid pharmacologic therapy, or nonpharmacologic therapy with respect to: (1) misuse, opioid use disorder, and related outcomes; (2) overdose; (3) other harms including gastrointestinal-related harms, falls, fractures, motor vehicle accidents, endocrinological harms, infections, cardiovascular events, cognitive harms, and psychological harms (e.g., depression)?

d. How do harms vary depending on: (1) patient demographics (e.g., age, gender); (2) patient medical or psychiatric comorbidities; (3) the dose of opioid used; (4) the duration of opioid therapy; (5) opioid use history; or (6) substance use history?

e. What are the effects of prescribing opioid therapy versus not prescribing opioid therapy for acute pain on 1) short-term (<3 months) continued need for prescription pain relief, such as need for opioid refills, and 2) long-term opioid use (3 months or greater)?

f. For patients with acute pain being considered for opioid therapy, what is the accuracy of instruments for predicting risk of opioid misuse, opioid use disorder, or overdose?

g. For patients with acute pain being considered for opioid therapy, what is the effectiveness of instruments for predicting risk of opioid misuse, opioid use disorder, or overdose?

h. For patients with acute pain being considered for opioid therapy, what is the effect of the following factors on the decision to prescribe opioids: (1) existing opioid management plans; (2) patient education; (3) clinician and patient values and preferences related to opioids; (4) urine drug screening; (5) use of prescription drug monitoring program data; (6) availability of close followup?

## Nonopioid Pharmacologic Therapy

i. What is the comparative effectiveness of nonopioid pharmacologic therapy (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs, antidepressants, anticonvulsants) versus: (1) other nonopioid pharmacologic treatments, such as those in a different medication class; or (2) nonpharmacologic therapy for outcomes related to pain, function, pain relief satisfaction, and quality of life after followup at the following intervals: <1 day; 1 day to <1 week; 1 week to <2 weeks; 2 weeks to less than 4 weeks; 4 weeks or longer?

j. How does effectiveness of nonopioid pharmacologic therapy vary depending on: (1) patient demographics (e.g., age, race, ethnicity, gender); (2) patient medical and psychiatric comorbidities; (3) the type of nonopioid medication; (4) dose of medication; (5) duration of treatment?

k. What are the harms of nonopioid pharmacologic therapy versus other nonopioid pharmacologic therapy or nonpharmacologic therapy with respect to: (1) misuse, (2) overdose; (3) other harms including gastrointestinal-related harms, cardiovascular-

related harms, kidney-related harms, falls, fractures, motor vehicle accidents, endocrinological harms, infections, cognitive harms, and psychological harms (e.g., depression)?

l. How do harms vary depending on: (1) patient demographics (e.g., age, gender); (2) patient medical comorbidities; (3) the type of nonopioid medication; (4) dose of medication; (5) the duration of therapy?

## Nonpharmacologic Therapy

m. What is the comparative effectiveness of nonpharmacologic therapy versus sham treatment, waitlist, usual care, attention control, and no treatment after followup at the following intervals: less than 1 day; 1 day to less than 1 week; 1 week to less than 2 weeks; 2 weeks to less than 4 weeks; 4 weeks or longer?

n. What is the comparative effectiveness of nonpharmacologic treatments (e.g., exercise, cognitive behavioral therapy, acupuncture) for outcomes related to pain, function, pain relief satisfaction, and quality of life after followup at the following intervals: less than 1 day; 1 day to less than 1 week; 1 week to less than 2 weeks; 2 weeks to less than 4 weeks; 4 weeks or longer?

o. How does effectiveness of nonpharmacologic therapy vary depending on: (1) patient demographics (e.g., age, gender); (2) patient medical and psychiatric comorbidities?

p. How do harms vary depending on: (1) patient demographics (e.g., age, gender); (2) patient medical and psychiatric comorbidities; (3) the type of treatment used; (4) the frequency of therapy; (5) the duration of therapy?

# Inclusion and Exclusion Criteria

**Table B-1. PICOTS: Inclusion and exclusion criteria**

| Picots Element | Include | Exclude |
|---|---|---|
| Population | Adults with acute pain related to the following conditions:<br>1. Acute back pain (including back pain with radiculopathy)<br>2. Acute neck pain (including neck pain with radiculopathy)<br>3. Other musculoskeletal pain<br>4. Peripheral neuropathic pain (related to herpes zoster and, trigeminal neuralgia)<br>5. Postoperative pain after discharge<br>6. Dental pain<br>7. Kidney stones<br>8. Sickle cell crisis (episodic pain)<br><br>*Special populations:<br>▪ General adult<br>▪ Older populations >65 years<br>▪ Patients with history of substance use disorder<br>▪ Patients currently under treatment for opioid use disorder with opioid agonist therapy or naltrexone<br>▪ Patients with a history of psychiatric illness<br>▪ Patients with history of overdose<br>▪ Pregnant/breastfeeding women<br>▪ Patients with comorbidities (e.g., kidney disease, sleep disordered breathing) | Adults with chronic (>3 months) and subacute pain (6 to 12 weeks); pain not associated with one of the 8 conditions; perioperative pain; children and adolescents (<18 years); headache and cancer pain, diabetic neuropathic pain, TMJ-related pain<br><br>Mixed chronic/acute or subacute/acute populations if study does not report separate results. |

| Picots Element | Include | Exclude |
|---|---|---|
| Interventions | **Opioid therapy:**<br>a-e. Any systemic opioid, including agonists, partial agonists, and mixed mechanism opioids.<br><br>f. Instruments, genetic/metabolic tests for predicting risk of misuse, opioid use disorder, and overdose<br>g. Use of risk prediction instruments, genetic/metabolic tests<br>h. The following factors: (1) existing opioid management plans; (2) patient education; (3) clinician and patient values and preferences related to opioids; (4) urine drug screening; (5) use of prescription drug monitoring program data; (6) availability of close followup<br>**Nonopioid pharmacological therapy:** Oral, parenteral, or topical nonopioid pharmacological therapy used for acute pain (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs, skeletal muscle relaxants, benzodiazepines, antidepressants, anticonvulsants, cannabis).<br>**Noninvasive nonpharmacological therapy:** Noninvasive nonpharmacological therapies used for acute pain (exercise [and related therapies], cognitive behavioral therapy, meditation, relaxation, music therapy, virtual reality, acupuncture, massage, manipulation/mobilization, physical modalities [transcutaneous electrical nerve stimulation, ultrasound, braces, traction, heat, cold]) | **Opioid therapy:**<br>a-e. Transdermal patches, topical opioids<br>f. Interventions to *treat* opioid use disorder, misuse, or overdose<br><br>h. Studies assessing these factors for effects *outside* of the decision to prescribe opioids<br><br>**Nonopioid pharm therapy:**<br>IV lidocaine; IV ketamine or other IV therapies *not* likely to continue in outpatient setting; all blocks; intra-articular injections; corticosteroids<br><br>**Noninvasive nonpharm therapy:**<br>Other therapies not listed |

| Picots Element | Include | Exclude |
|---|---|---|
| Comparators | **Opioid therapy:**<br>a-d. Usual care, another opioid, nonopioid drug, or noninvasive, nonpharmacological therapy<br>e. Usual care, another opioid, nonopioid drug, or noninvasive, nonpharmacological therapy, no opioid/nothing prescribed<br>f. Reference standard for misuse, opioid use disorder, or overdose; or other benchmarks<br>g. Usual care<br>h. Not utilizing the factors specified in interventions (h) above<br>**Nonopioid pharmacological therapy:**<br>Other nonopioid pharmacological therapy or noninvasive nonpharmacological therapy<br>**NOTE:** Include oral vs. topical NSAID studies as well as aspirin vs. NSAID studies<br>**Noninvasive nonpharmacological therapy:**<br>Sham treatment, waitlist, usual care, attention control, and no treatment; or other noninvasive nonpharmacological therapy | **Opioid therapy:**<br>a-d. other comparisons; placebo; included therapies vs. excluded therapies; dose ranging studies<br><br>**Nonopioid pharm therapy:**<br>placebo; included therapies vs. excluded therapies; dose ranging studies; NSAID vs. NSAID studies; selective NSAIDs vs. non-selective NSAIDs<br><br>**Noninvasive nonpharm therapy:**<br>historical controls; included therapies vs. excluded therapies |
| Outcomes | **Opioid therapy:**<br>a-d, g, i. Pain, function, pain relief satisfaction, and quality of life, harms, adverse events (including withdrawal, risk of misuse, opioid, opioid use disorder, overdose).<br>e. Persistent opioid use<br>f. Measures of diagnostic accuracy<br>h. Opioid prescribing rates<br>**Nonopioid therapy:** pain, function, pain relief satisfaction, quality of life and quality of life, harms, adverse events, opioid use<br>**Noninvasive nonpharmacological therapy:** pain, function, pain relief satisfaction, quality of life and quality of life, harms, adverse events, opioid use | Other outcomes; nonclinical outcomes (e.g., non-harm lab measures, ROM); measures of utilization (i.e., costs, procedures, length of stay, cost effectiveness/modeling) |
| Time of followup | At the following intervals: <1 day; 1 day to <1 week; 1 week to <2 weeks; 2 weeks to 4 weeks; ≥4 weeks<br>**NOTE:** There will not be exclusion criteria for duration, unless duration is a matter of minutes. | |
| Setting | Emergency department (initiation of therapy and following discharge), physician's office, outpatient or inpatient surgical center, dental clinic or oral surgery center, inpatient (sickle cell only) | Other settings |

| Picots Element | Include | Exclude |
|---|---|---|
| Study design | All KQs: RCTs; in addition:<br>e. cohort studies (for long-term opioid use)<br>f. studies assessing diagnostic accuracy<br>h. cohort studies and before-after studies assessing effects on prescribing rates | For all KQs, exclude uncontrolled observational studies, case series, and case reports; studies with historical controls |

Abbreviations: IV = intravenous; KQ = Key Question; NSAID = nonsteroidal anti-inflammatory drug; PICOTS = population, interventions, comparators, outcomes, timing, setting, study design; RCT = randomized controlled trial; ROM = range of motion; TMJ = temporomandibular joints

# Appendix C. Included Studies List


1. Akgol Gur ST, Dogruyol S, Kocak AO, et al. Topical capsaicin versus topical ibuprofen in acute musculoskeletal injuries: a randomized, double-blind trial. Hong Kong Journal of Emergency Medicine. 2020;00(0):1-7. doi: 10.1177/1024907920975368.

2. Bloom DA, Kirby DJ, Thompson K, et al. Effect of acetaminophen on postoperative percocet use in hip arthroscopy: a randomized controlled trial. Arthroscopy. 2021;37(2):530-6. doi: 10.1016/j.arthro.2020.09.046. PMID: 33045334.

3. Brouwers HFG, de Vries AJ, van Zuilen M, et al. The role of computer-assisted cryotherapy in the postoperative treatment after total knee arthroplasty: positive effects on pain and opioid consumption. Knee Surg Sports Traumatol Arthrosc. 2021 doi: 10.1007/s00167-021-06568-x. PMID: 33903923.

4. Cooper SA, Desjardins PJ, Bertoch T, et al. Analgesic efficacy of naproxen sodium versus hydrocodone/acetaminophen in acute postsurgical dental pain: a randomized, double-blind, placebo-controlled trial. Postgrad Med. 2021:1-8. doi: 10.1080/00325481.2021.2008180. PMID: 34878953.

5. Cope AG, Wetzstein MM, Mara KC, et al. Abdominal ice after laparoscopic hysterectomy: a randomized controlled trial. J Minim Invasive Gynecol. 2021;28(2):342-50.e2. doi: 10.1016/j.jmig.2020.06.027. PMID: 32622918.

6. da Silva PB, Mendes AT, Cardoso MBF, et al. Comparison between isolated and associated with codeine acetaminophen in pain control of acute apical abscess: a randomized clinical trial. Clin Oral Investig. 2021;25(3):875-82. doi: 10.1007/s00784-020-03374-6. PMID: 32651644.

7. Desjardins P, Alvarado F, Gil M, et al. Efficacy and safety of two fixed-dose combinations of tramadol hydrochloride and diclofenac sodium in postoperative dental pain. Pain Med. 2020;21(10):2447-57. doi: 10.1093/pm/pnaa124. PMID: 32488263.

8. Frants A, Garber D, Lafer MP, et al. Prospective randomized trial comparing opioids versus nonsteroidal antiinflammatory drugs for postoperative analgesia in outpatient rhinoplasty. Plast Reconstr Surg. 2021;147(1):56-62. doi: 10.1097/PRS.0000000000007427. PMID: 33370050.

9. Friedman BW, Irizarry E, Feliciano C, et al. A randomized controlled trial of oxycodone/acetaminophen versus acetaminophen alone for emergency department patients with musculoskeletal pain refractory to ibuprofen. Acad Emerg Med. 2021;28(8):859-65. doi: 10.1111/acem.14231. PMID: 33576545.

10. Hoskins C, Dempsey A, Brou L. A mixed-methods study of the effect of abdominal binders on opioid use and postoperative pain after cesarean birth. Nurs Womens Health. 2022;S1751-4851(21):00253-1. doi: 10.1016/j.nwh.2021.12.002. PMID: 35032465.

11. Ilyas AM, Chapman T, Zmistowski B, et al. The effect of preoperative opioid education on opioid consumption after outpatient orthopedic surgery: a prospective randomized trial. Orthopedics. 2021;44(2):123-7. doi: 10.3928/01477447-20210201-07. PMID: 33561870.

12. Laframboise-Otto JM, Horodyski M, Parvataneni HK, et al. A randomized controlled trial of music for pain relief after arthroplasty surgery. Pain Manag Nurs. 2021;22(1):86-93. doi: 10.1016/j.pmn.2020.09.003. PMID: 33129705.

13. Parseliunas A, Paskauskas S, Kubiliute E, et al. Transcutaneous electric nerve stimulation reduces acute postoperative pain and analgesic use after open inguinal hernia surgery: a randomized, double-blind, placebo-controlled trial. J Pain. 2021;22(5):533-44. doi: 10.1016/j.jpain.2020.11.006. PMID: 33309784.

14. Paskey T, Vincent S, Critchlow E, et al. Prospective randomized study evaluating the effects of preoperative opioid counseling on postoperative opioid use after outpatient

lower extremity orthopaedic surgery. J Surg Orthop Adv. 2021;30(1):2-6. PMID: 33851905.

15. Rian T, Skogvoll E, Hofstad J, et al. Tapentadol vs oxycodone for postoperative pain treatment the first 7 days after total knee arthroplasty: a randomized clinical trial. Pain. 2021;162(2):396-404. doi: 10.1097/j.pain.0000000000002026. PMID: 32773594.

16. Skonnord T, Skjeie H, Brekke M, et al. Acupuncture for acute non-specific low back pain: a randomised, controlled, multicentre intervention study in general practice - the Acuback study. BMJ Open. 2020;10(8):e034157. doi: 10.1136/bmjopen-2019-034157. PMID: 32764081.

17. Suwannalert P, Chanthasenanont A, Pongrojpaw D. Effect of applying cold gel pack on reduction of postoperative pain in cesarean section, low midline skin incision: a randomized controlled trial. J Obstet Gynaecol Res. 2021;47(8):2653-8. doi: 10.1111/jog.14855. PMID: 34008228.

18. Thota L, Bansal R, Thota G, et al. Efficacy of routinely used analgesics in management of pulpal pain postoperatively a clinical study. J Pharm Bioallied Sci. 2021;13(Suppl 1):S684-S7. doi: 10.4103/jpbs.JPBS_782_20. PMID: 34447181.

19. Vallecillo C, Vallecillo-Rivas M, Galvez R, et al. Analgesic efficacy of tramadol/dexketoprofen vs ibuprofen after impacted lower third molar extraction: a randomized controlled clinical trial. J Evid Based Dent Pract. 2021;21(4):101618. doi: 10.1016/j.jebdp.2021.101618. PMID: 34922724.

20. Zhu CY, Schumm MA, Hu TX, et al. Patient-centered decision-making for postoperative narcotic-free endocrine surgery: a randomized clinical trial. JAMA Surg. 2021:e214287. doi: 10.1001/jamasurg.2021.4287. PMID: 34495283.

# Appendix D. Excluded Studies List

1. Abo Elfadl GM, Osman AM, Ghalyoom MF, et al. Preoperative duloxetine to prevent postoperative shoulder pain after gynecologic laparoscopy: a randomized controlled trial. Braz J Anesthesiol. 2021 doi: 10.1016/j.bjane.2021.07.035. PMID: 34411629. **Exclusion reason:** Ineligible population
2. Abushanab D, Al-Badriyeh D. Efficacy and safety of ibuprofen plus paracetamol in a fixed-dose combination for acute postoperative pain in adults: meta-analysis and a trial sequential analysis. CNS Drugs. 2021;35(1):105-20. doi: 10.1007/s40263-020-00777-7. PMID: 33428176. **Exclusion reason:** Paper pulled for background
3. A comparison of clinic-delivered and telehealth-delivered post-operative rehabilitation and functional assessment following total knee arthroplasty. http://www.who.int/trialsearch/Trial2.aspx?TrialID=ACTRN12620001168943. 2020. **Exclusion reason:** Ineligible publication type/not a study (letter, editorial, non-systematic review article, no original data)
4. Akdogan M, Utebey G, Atilla HA, et al. Effects of preoperative pregabalin on postoperative pain control in total knee arthroplasty surgery. J Invest Surg. 2021;34(8):848-52. doi: 10.1080/08941939.2019.1704317. PMID: 31913778. **Exclusion reason:** Ineligible intervention
5. Akpinar KE, Kaya F. Effect of different clinical practices on postoperative pain in permanent mandibular molar teeth with symptomatic apical periodontitis: a randomized controlled clinical trial. Niger J Clin Pract. 2021;24(1):8-16. doi: 10.4103/njcp.njcp_16_20. PMID: 33473019. **Exclusion reason:** Ineligible intervention
6. Almasri M, Simunovic N, Heels-Ansdell D, et al. Femoroacetabular impingement surgery leads to early pain relief but minimal functional gains past 6 months: experience from the FIRST trial. Knee Surg Sports Traumatol Arthrosc. 2021;29(5):1362-9. doi: 10.1007/s00167-020-06401-x. PMID: 33386426. **Exclusion reason:** Ineligible intervention
7. Alshahrani M, Alghamdi M. Ketamine for sickle cell vaso-occlusive crises: a systematic review. Saudi J Med Med Sci. 2021;9(1):3-9. doi: 10.4103/sjmms.sjmms_218_20. PMID: 33519337. **Exclusion reason:** Paper pulled for background
8. Alzahrani H, Mackey M, Stamatakis E, et al. Wearables-based walking program in addition to usual physiotherapy care for the management of patients with low back pain at medium or high risk of chronicity: a pilot randomized controlled trial. PLoS One. 2021;16(8):e0256459. doi: 10.1371/journal.pone.0256459. PMID: 34437607. **Exclusion reason:** Ineligible population
9. Anger M, Valovska T, Beloeil H, et al. PROSPECT guideline for total hip arthroplasty: a systematic review and procedure-specific postoperative pain management recommendations. Anaesthesia. 2021;76(8):1082-97. doi: 10.1111/anae.15498. PMID: 34015859. **Exclusion reason:** Inadequate duration
10. Ansari AH, Shooshtari Z, Alipour M, et al. What is the effect of pre-emptive oral montelukast on postoperative pain following bimaxillary orthognathic surgery? A triple-blind randomized clinical trial. J Oral Maxillofac Surg. 2021;20:20. doi: 10.1016/j.joms.2021.08.151. PMID: 34547261. **Exclusion reason:** Ineligible intervention
11. Antony KM, Adams JH, Jacques L, et al. Lidocaine patches for postcesarean pain control in obese women: a pilot randomized controlled trial. Am J Obstet Gynecol MFM. 2021;3(1):100281. doi: 10.1016/j.ajogmf.2020.100281. PMID: 33451596. **Exclusion reason:** Ineligible comparator
12. Anusitviwat C, Suwanno P, Suwannaphisit S. The effects of vitamin D supplementation in carpal tunnel syndrome treatment outcomes: a systematic review. J Exp Orthop. 2021;8(1)doi: 10.1186/s40634-021-00393-4. **Exclusion reason:** Ineligible intervention
13. Attaar A, Curran M, Meyenburg L, et al. Perioperative pain management and

outcomes in patients who -discontinued or continued pre-existing buprenorphine therapy. J Opioid Manag. 2021;17(7):33-41. doi: 10.5055/jom.2021.0640. PMID: 34520024. **Exclusion reason:** Ineligible intervention

14. Bebee B, Taylor DM, Bourke E, et al. The CANBACK trial: a randomised, controlled clinical trial of oral cannabidiol for people presenting to the emergency department with acute low back pain. Med J Aust. 2021;214(8):370-5. doi: 10.5694/mja2.51014. PMID: 33846971. **Exclusion reason:** Ineligible population

15. Bigalke S, Maesen TV, Schnabel K, et al. Assessing outcome in postoperative pain trials: are we missing the point? A systematic review of pain-related outcome domains reported in studies early after total knee arthroplasty. Pain. 2021;162(7):1914-34. doi: 10.1097/j.pain.0000000000002209. PMID: 33492036. **Exclusion reason:** Ineligible intervention

16. Bijur PE, Friedman BW, Irizarry E, et al. A randomized trial comparing the efficacy of five oral analgesics for treatment of acute musculoskeletal extremity pain in the emergency department. Ann Emerg Med. 2021;77(3):345-56. doi: 10.1016/j.annemergmed.2020.10.004. PMID: 33358232. **Exclusion reason:** Ineligible intervention

17. Bloom DA, Baron SL, Luthringer TA, et al. Preoperative opioid education has no effect on opioid use in patients undergoing arthroscopic rotator cuff repair: a prospective, randomized clinical trial. J Am Acad Orthop Surg 2021;29(19):e961-e8. doi: 10.5435/JAAOS-D-20-00594. PMID: 33306558. **Exclusion reason:** Ineligible outcome

18. Bloom DA, Manjunath AK, Gotlin MJ, et al. Institutional reductions in opioid prescribing do not change patient satisfaction on Press Ganey surveys after total shoulder arthroplasty. J Shoulder Elbow Surg. 2021;30(4):858-64. doi: 10.1016/j.jse.2020.07.016. PMID: 32712454. **Exclusion reason:** Ineligible outcome

19. Bloom DA, Manjunath AK, Gualtieri AP, et al. Patient satisfaction after total hip arthroplasty is not influenced by reductions in opioid prescribing. J Arthroplasty. 2021;36(7S):S250-S7. doi: 10.1016/j.arth.2021.02.009. PMID: 33640183. **Exclusion reason:** Ineligible comparator

20. Bloom DA, Manjunath AK, Kaplan DJ, et al. Reduced opioid prescribing following arthroscopic meniscectomy does not negatively impact patient satisfaction. Knee. 2021;29:216-21. doi: 10.1016/j.knee.2021.01.020. PMID: 33640620. **Exclusion reason:** Ineligible comparator

21. Bojaxhi E, Louie C, ReFaey K, et al. Reduced pain and opioid use in the early postoperative period in patients undergoing a frontotemporal craniotomy under regional vs general anesthesia. World Neurosurg. 2021;150:e31-e7. doi: 10.1016/j.wneu.2021.02.009. PMID: 33684585. **Exclusion reason:** Ineligible population

22. Bornstein E, Husk G, Lenchner E, et al. Implementation of a standardized post-cesarean delivery order set with multimodal combination analgesia reduces inpatient opioid usage. J Clin Med. 2021;10(1):1-10. doi: 10.3390/jcm10010007. **Exclusion reason:** Ineligible comparator

23. Brady JT, Dreimiller A, Miller-Spalding S, et al. Are narcotic pain medications necessary after discharge following thyroidectomy and parathyroidectomy? Surgery. 2021;169(1):202-8. doi: 10.1016/j.surg.2020.03.027. PMID: 32416981. **Exclusion reason:** Ineligible intervention

24. Burns KA, Robbins LM, LeMarr AR, et al. Celecoxib significantly reduces opioid use after shoulder arthroplasty. J Shoulder Elbow Surg. 2021;30(1):1-8. doi: 10.1016/j.jse.2020.08.025. PMID: 32919045. **Exclusion reason:** Ineligible comparator

25. Buys MJ, Bayless K, Romesser J, et al. Opioid use among veterans undergoing major joint surgery managed by a multidisciplinary transitional pain service. Reg Anesth Pain Med. 2020;45(11):847-52. doi: 10.1136/rapm-2020-101797. PMID: 32848086. **Exclusion reason:** Ineligible intervention

26. Cashin AG, Folly T, Bagg MK, et al. Efficacy, acceptability, and safety of muscle relaxants for adults with non-specific low back pain: systematic review and meta-analysis. BMJ. 2021;374:n1446. doi: 10.1136/bmj.n1446. PMID: 34233900. **Exclusion reason:** Paper pulled for background

27. Chen W, Sun JN, Hu ZH, et al. Cognitive behavioral therapy cannot relieve postoperative pain and improve joint function after total knee arthroplasty in patients aged 70 years and older. Aging Clin Exp Res. 2021 doi: 10.1007/s40520-021-01870-7. PMID: 33991330. **Exclusion reason:** Ineligible population

28. Cheng X, Wang Z, Zhang Y, et al. Oral administration of prednisone effectively reduces subacute pain after total knee arthroplasty. Orthop Traumatol Surgery Res. 2021;107(3):102770. doi: 10.1016/j.otsr.2020.102770. PMID: 33333285. **Exclusion reason:** Ineligible intervention

29. A multicenter, randomized, double-blind, placebo-controlled parallel clinical trial to evaluate the efficacy and safety of ibuprofen injection in the treatment of postoperative acute pain. http://www.who.int/trialsearch/Trial2.aspx?TrialID=ChiCTR2100042038. 2021. **Exclusion reason:** Ineligible publication type/not a study (letter, editorial, non-systematic review article, no original data)

30. Chou R, Dana T, Shetty KD. Testing a machine learning tool for facilitating living systematic reviews of chronic pain treatments. Methods Research Report. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290- 2015-00009-I and the Southern California Evidence-based Practice Center-RAND Corporation under Contract No. 290-2015-00010-I.) AHRQ Publication No. 21-EHC004. Rockville, MD: Agency for Healthcare Research and Quality November 2020. **Exclusion reason:** Paper pulled for background

31. Chou R, Wagner J, Ahmed AY, et al. Treatments for acute pain: a systematic review. Comparative Effectiveness Review No 240. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290- 2015-00009-I.) AHRQ Publication No. 20(21)-EHC006. Rockville, MD: Agency for Healthcare Research and Quality; December 2020. **Exclusion reason:** Paper pulled for background

32. Choudhry NK, Fontanet CP, Ghazinouri R, et al. Design of the spine pain intervention to enhance care quality and reduce expenditure trial (SPINE CARE) study: methods and lessons from a multi-site pragmatic cluster randomized controlled trial. Contemp Clin Trials. 2021;111:106602. doi: 10.1016/j.cct.2021.106602. PMID: 34688915. **Exclusion reason:** Ineligible publication type/not a study (letter, editorial, non-systematic review article, no original data)

33. Chuaychoosakoon C, Parinyakhup W, Wiwatboworn A, et al. Comparing post-operative pain between single bundle and double bundle anterior cruciate ligament reconstruction: a retrospective study. BMC Musculoskelet Disord. 2021;22(1):753. doi: 10.1186/s12891-021-04635-5. PMID: 34479511. **Exclusion reason:** Ineligible intervention

34. Comelon M, Raeder J, Draegni T, et al. Tapentadol versus oxycodone analgesia and side effects after laparoscopic hysterectomy: a randomised controlled trial. Eur J Anaesthesiol. 2021;38(9):995-1002. doi: 10.1097/EJA.0000000000001425. PMID: 33428347. **Exclusion reason:** Ineligible population

35. Cooper TE, Hambleton IR, Ballas SK, et al. Pharmacological interventions for painful sickle cell vaso-occlusive crises in adults. Cochrane Database Syst Rev. 2019;2019(11):CD012187. doi: 10.1002/14651858.CD012187.pub2. PMID: 31742673. **Exclusion reason:** Paper pulled for background

36. Electro acupuncture therapy on carpal tunnel syndrome. http://www.who.int/trialsearch/Trial2.aspx?TrialID=CTRI. 2020. **Exclusion reason:** Ineligible publication type/not a study (letter, editorial, non-systematic review article, no original data)

37. Dalton MK, Chaudhary MA, Andriotti T, et al. Patterns and predictors of opioid prescribing and use after rib fractures.

Surgery. 2020;168(4):684-9. doi: 10.1016/j.surg.2020.05.015. PMID: 32653204. **Exclusion reason:** Ineligible intervention

38. Davey MS, Hurley ET, Anil U, et al. Pain management strategies after anterior cruciate ligament reconstruction: a systematic review with network meta-analysis. Arthroscopy. 2021;37(4):1290-300.e6. doi: 10.1016/j.arthro.2021.01.023. PMID: 33515736. **Exclusion reason:** Ineligible intervention

39. Davidson ERW, Paraiso MFR, Walters MD, et al. A randomized controlled noninferiority trial of reduced vs routine opioid prescription after prolapse repair. Am J Obstet Gynecol. 2020;223(4):547.e1-.e12. doi: 10.1016/j.ajog.2020.03.017. PMID: 32199926. **Exclusion reason:** Paper pulled for background

40. de Oliveira Lima L, Saragiotto BT, Costa LOP, et al. Self-guided web-based pain education for people with musculoskeletal pain: a systematic review and meta-analysis. Phys Ther. 2021;101(10):01. doi: 10.1093/ptj/pzab167. PMID: 34174081. **Exclusion reason:** Ineligible population

41. de Queiroz VKP, da Nobrega Marinho AM, de Barros GAM. Analgesic effects of a 5% lidocaine patch after cesarean section: a randomized placebo-controlled double-blind clinical trial. J Clin Anesth. 2021;73:110328. doi: 10.1016/j.jclinane.2021.110328. PMID: 33975094. **Exclusion reason:** Ineligible comparator

42. Delavar P, Foroughian M, Vakilzadeh AK, et al. Effect of acupuncture on the pain of patients with acute low back pain: a randomized double-blind clinical trial study. Koomesh. 2021;23(3):338-46. doi: 10.29252/koomesh.23.3.338. **Exclusion reason:** Study covered in included systematic review

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# Appendix E. Evidence Tables

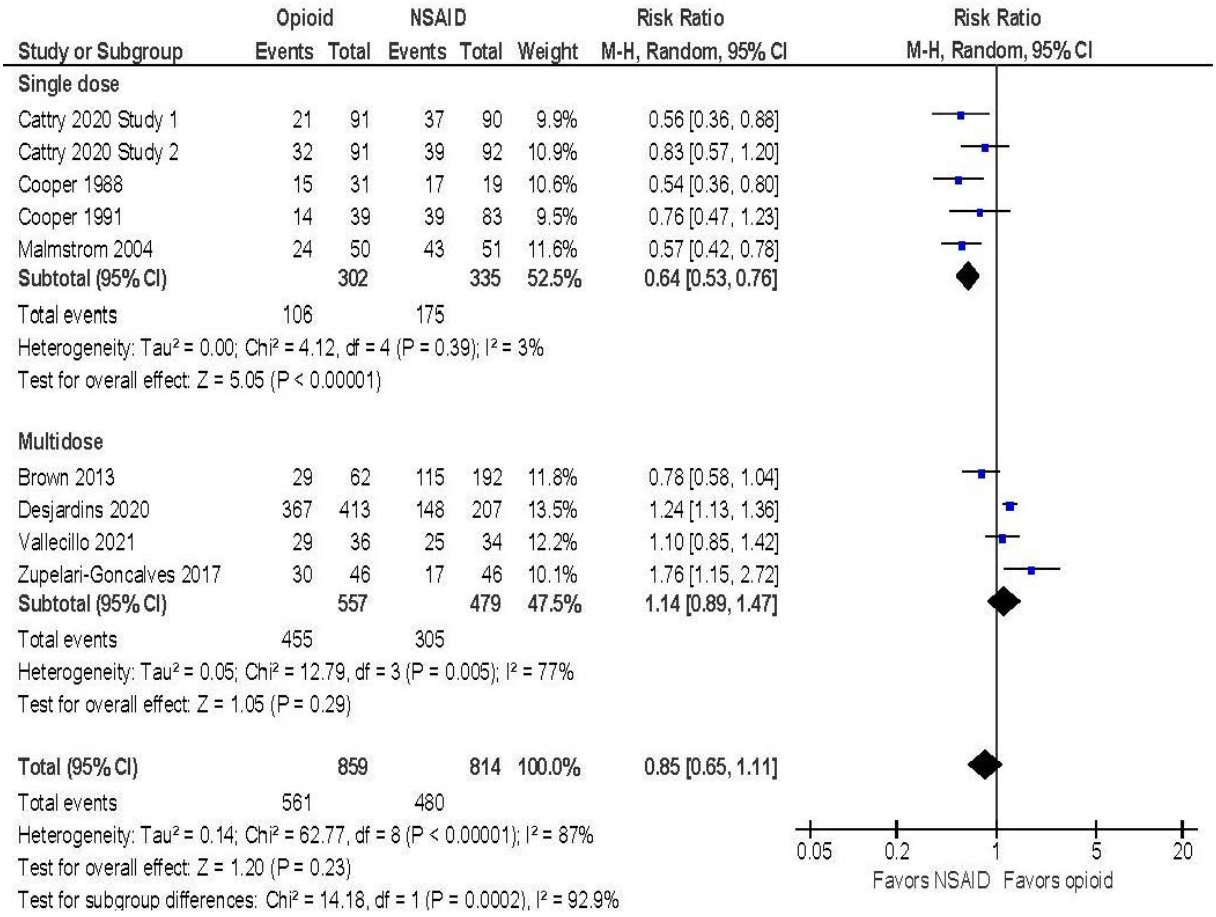
Shown in associated Excel file for Surveillance Report 2 at https://effectivehealthcare.ahrq.gov/products/treatments-acute-pain/research

# Appendix F. Quality Assessment

Shown in associated Excel file for Surveillance Report 2 at https://effectivehealthcare.ahrq.gov/products/treatments-acute-pain/research.

# Appendix G. Meta-Analysis Results

**Figure G-1. Meta-analysis: opioid versus NSAID for global improvement**




Abbreviations: NSAID = nonsteroidal anti-inflammatory drug