

Acute Pain Management: Non-Opioid Treatments (Pharmacologic and Non-Pharmacologic)

Canada is in the midst of an opioid crisis. Like many organizations across the country, CADTH has made addressing the opioid crisis a top priority. In the last year, we have delivered a large body of evidence to inform decisions on effectively treating opioid use disorder and how we use drug and non-drug interventions to help patients manage pain. But in doing so, we've also revealed some significant gaps in the evidence — areas where evidence is needed but where little or no high-quality evidence can be found.

Knowing where these gaps in the evidence exist can help researchers and research funding bodies better focus their efforts on opioid research and the management of pain.

Following, you'll find a list of gaps in evidence related to the treatment of acute pain with non-opioid pharmacologic or non-pharmacologic options that we've identified while carrying out recent rapid reviews through our **Rapid Response Service**. For the treatment of acute pain with opioids, please see our related publication on *Opioids for the Treatment of Pain*.

Other publications in this series will highlight gaps in areas also important to the opioid crisis including *Treating Opioid Use Disorder*, *Opioids for the Treatment of Pain*, *Chronic Pain Management: Pharmacologic Treatments (Non-Opioids)*, and *Chronic Pain Management: Non-Pharmacologic Treatments*.

For more information about the CADTH response to the opioid crisis and our evidence, please visit cadth.ca/opioids and cadth.ca/pain.

It's important to note that these gaps in evidence have been compiled from multiple CADTH reports from 2014 to the end of 2017. For more details on each identified gap, consulting the full CADTH report is highly recommended. Depending on the date of the report, additional evidence may now be available that addresses the research gaps, as well as evidence from other organizations. And because of the methods used for rapid reviews, it is possible that evidence that could potentially address the research gaps may not have been included.

Manual Therapy for Recent-Onset or Persistent Neck Pain (2017)

Evidence Requested for Decision-Making

- Clinical effectiveness of manual therapy for recent-onset or persistent neck pain in adult or pediatric patients
- Recommendations from evidence-based guidelines regarding manual therapy for recent-onset or persistent neck pain in adults or pediatric patients

What We Found

- Manipulation and mobilization appear to be effective for managing neck pain in adults.
- Massage may be beneficial for managing neck pain in adults.
- Traction may be beneficial for managing neck pain in adults, but this evidence is of limited quality.
- Two evidence-based guidelines recommend the use of manual therapies for acute and chronic neck pain in adults including manipulation, mobilization, multimodal manual therapy, and massage.
- The guidelines both recommend not to use relaxation massage, strain-counterstrain therapy, and/or traction.

Evidence Gaps

What We Did Not Find

Sufficient high-quality studies — authors should provide additional details regarding the type of manual therapy procedure, as well as the frequency and duration of treatments

Longer-term studies

Research evaluating the clinical effectiveness of manual therapy in the pediatric population

Recommendations from evidence-based guidelines specific to the pediatric population

Manual Therapy for Recent-Onset or Persistent Non-Specific Lower Back Pain (2017)

Evidence Requested for Decision-Making

- Clinical effectiveness of manual therapy for recent-onset or persistent non-specific lower back pain in adults or pediatric patients
- Recommendations from evidence-based guidelines regarding manual therapy for recent-onset or persistent non-specific lower back pain in adult or pediatric patients

What We Found

- Low-quality evidence suggests that spinal manipulation and soft tissue therapy may have positive effects on pain and function for acute and chronic low back pain.
- The effectiveness of spinal mobilization (often included as an adjunct to spinal manipulation) is uncertain.
- Traction for low back pain with or without radiculopathy appears **not** to be effective.
- No serious harms have been reported.
- Three evidence-based guidelines provided recommendations supporting the use of manual therapy (including spinal manipulation) for acute and chronic low back pain in adults.
- One guideline recommended **against** the use of traction.

Evidence Gaps

What We Did Not Find

Sufficient high-quality research — authors should provide more detailed information regarding the type of procedure utilized and the dosage of treatments

Research evaluating the clinical effectiveness and safety of manual therapies in the pediatric population

Recommendations from evidence-based guidelines specific to the pediatric population

Physiotherapy Interventions for the Management of Neck and/or Back Pain (2017)

Evidence Requested for Decision-Making

- Clinical effectiveness of physiotherapy interventions for the management of neck and/or back pain
- Cost-effectiveness of physiotherapy interventions for the management of neck and/or back pain

What We Found

- Physiotherapy for neck and/or back pain appears to be effective or, at the very least, neutral.
- The body of evidence was limited and largely low to moderate in quality; no adverse effects were reported.

Evidence Gaps

What We Did Not Find

High-quality research regarding the clinical effectiveness of physiotherapy for the management of neck and/or back pain (including adverse event reporting)

Studies comparing the clinical effectiveness of physiotherapy to opioids

Evidence on the cost-effectiveness of physiotherapy for the management of neck and/or back pain

The Use of Medical Cannabis With Other Medications (2017)

Evidence Requested for Decision-Making

- Clinical evidence regarding the safety of medical cannabis when used concurrently with other medications
- Recommendations from evidence-based guidelines regarding the use of medical cannabis with other medications

What We Found

- Medical cannabis (Nabilone) may have additive depressant effects with diazepam when taken together with alcohol and codeine.
- Medical cannabis may decrease the need for opioids, NSAIDs, tricyclic antidepressants, dexamethasone and ondansetron when used concomitantly.

Evidence Gaps

What We Did Not Find

High-quality research

Data on the drug interactions of medical cannabis with other medications

Recommendations from evidence-based guidelines

NSAID = nonsteroidal anti-inflammatory drug.

Pregabalin for Acute Pain (2017)

Evidence Requested for Decision-Making

- Clinical effectiveness of pregabalin for acute pain
- Clinical effectiveness of pregabalin and opioids compared with opioids alone for managing acute or post-operative pain

What We Found

- Compared with opioids alone, a single dose of pregabalin used pre-operatively in combination with post-operative opioids may reduce post-operative opioid consumption, pain scores, and the use of breakthrough analgesia at 48 hours.
- Pregabalin may reduce pain (neuropathic and procedural) in patients with severe burn injuries compared with placebo.
- A single dose of pregabalin does not appear to decrease acute pain secondary to herpes zoster compared with placebo.
- There was no significant increase in adverse effects associated with pregabalin.

Evidence Gaps

What We Did Not Find

Sufficient high-quality research

Longer-term studies with larger sample sizes

Evidence specific to various types of acute pain, various age groups, and patients with underlying medical or psychiatric illness including substance use disorders

Evidence comparing the use of pregabalin in combination with opioids to opioids alone for the management of acute non-surgical pain

Topical NSAIDs Versus Opioids for Acute Musculoskeletal Pain (2017)

Evidence Requested for Decision-Making

- Clinical effectiveness of topical NSAIDs compared with opioids for acute musculoskeletal pain

What We Found

- Topical NSAIDs are effective in reducing pain from acute musculoskeletal conditions such as sprains, strains, or sports injuries compared with placebo.
- Adverse events were rare and were usually related to skin reactions.

Evidence Gaps

What We Did Not Find

High-quality research specific to various pain conditions and to various age groups (included studies were limited to strains, sprains, or sports injuries in healthy adults from 25- to 57-year-olds who were actively engaged in sports)

Evidence assessing the clinical effectiveness of topical NSAIDs compared with opioids in acute musculoskeletal pain

Evidence assessing the clinical effectiveness of topical NSAIDs as an adjunct to opioids in acute musculoskeletal pain

Evidence assessing the effect of topical NSAIDs on reduction in opioid use or dose

Evidence assessing quality of life

NSAID = nonsteroidal anti-inflammatory drug.

1,000 mg Versus 650 mg Acetaminophen for Pain or Fever (2016)

Evidence Requested for Decision-Making

- Clinical effectiveness of 1,000 mg compared with 650 mg or 600 mg of acetaminophen for pain
- Clinical effectiveness of 1,000 mg compared with 650 mg or 600 mg of acetaminophen for fever

What We Found

- Pain relief may be improved with 1,000 mg of acetaminophen compared with 650 mg of acetaminophen in various acute post-operative pain conditions.
- The risk of adverse events was similar between the two doses, with no serious adverse events reported.

Evidence Gaps

What We Did Not Find

More high-quality research on the comparative efficacy and safety of 1,000 mg versus 650 mg of acetaminophen

Evidence specific to various pain conditions (included studies were limited to post-surgical pain conditions, only)

More studies evaluating the currently recommended maximum daily dose of acetaminophen (4 g) and the long-term use of acetaminophen

Evidence comparing the clinical efficacy of 1,000 mg with 650 mg of acetaminophen to manage fever

Interventions for Atypical Facial Pain (2016)

Evidence Requested for Decision-Making

- Clinical effectiveness of pharmacological and non-pharmacological interventions for patients with atypical facial pain
- Evidence-based guidelines regarding interventions for patients with atypical facial pain

What We Found

- Low-quality studies on surgical procedures reported generally poor outcomes related to pain relief and complications or adverse events.
- Low-quality studies on non-surgical (drug and non-drug) options were found to attenuate pain symptoms in some patients but not in all.
- One guideline recommended pharmacologic agents as first-line treatment, followed by minimally invasive surgical intervention, for patients who do not respond to drug therapy.

Evidence Gaps

What We Did Not Find

**High-quality research
(large prospective studies with
appropriate randomization)**

**Studies on the effectiveness
of non-surgical interventions
(drug and non-drug) in alleviating
pain and minimizing treatment-
related complications in patients
with atypical facial pain**

Canadian studies

**Recommendations from guidelines
that are based on high-quality
studies**

Prolotherapy for the Management of Musculoskeletal Pain (2014)

Evidence Requested for Decision-Making

- Clinical effectiveness and safety of prolotherapy for the management of musculoskeletal pain

What We Found

- Low-quality evidence suggests dextrose prolotherapy for musculoskeletal pain (including low back pain, tendinopathy, and osteoarthritis) may provide pain relief and improve physical function compared with saline injection control, exercise alone, or before prolotherapy treatment.

Evidence Gaps

What We Did Not Find

High-quality studies (addressing the limitations of the current body of evidence)

Longer-term studies with larger sample sizes, optimized and consistent techniques/procedures, and validated outcomes measures

Evidence on the effectiveness of prolotherapy compared with corticosteroid injections

Ketamine for Adult Patients Who Have Suffered Painful and Traumatic Injuries (2014)

Evidence Requested for Decision-Making

- Clinical effectiveness and safety of ketamine in adult patients who have suffered painful and traumatic brain or eye injury
- Optimal dose of ketamine (IV, IM, and intranasally) and safety in adults with moderate to severe pain from traumatic injury who are conscious
- Safety issues regarding the use of ketamine at low doses when compared with fentanyl and morphine for adults with moderate-to-severe pain from traumatic injury
- Cost-effectiveness of using ketamine for adult patients who have suffered painful and traumatic brain or eye injury
- Guidelines associated with the use of ketamine for adult patients who have suffered painful and traumatic brain or eye injury

What We Found

- One study (post hoc analysis) failed to show a difference between ketamine and morphine for analgesic effect in a subset of patients with head trauma.

Evidence Gaps

What We Did Not Find

High-quality research examining the clinical effectiveness and safety of ketamine (monotherapy) in adult patients with painful and traumatic eye injury (no published trials were identified)

Studies on the optimal dose of ketamine (and any safety issues with the doses) in adults with moderate-to-severe pain from traumatic injury who are conscious

Studies on the safety of ketamine compared with fentanyl and morphine in adults with moderate-to-severe pain from traumatic injury

Economic evaluations on ketamine in patients with painful and traumatic brain or eye injury

Recommendation from evidence-based guidelines on the use of ketamine in patients with painful and traumatic brain or eye injury

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ABOUT CADTH

CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs and medical devices in our health care system.

CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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