RESEARCH GAPS | Improving the Evidence

Treating Opioid Use Disorder

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 opioid use disorder that we've identified while carrying out recent rapid reviews through our **Rapid Response Service.**

Other publications in this series will highlight gaps in areas also important to the opioid crisis, including opioid misuse, overdose, and harms; opioids and the treatment of pain; alternatives to opioids; chronic pain management; and acute pain management.

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 2015 to the end of 2019. 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 gap. Evidence from other organizations may also be available that could address the research gaps. Because of the methods used for rapid reviews, it is possible that evidence may not have been included that could potentially address the research gaps.

CADTH

Buprenorphine-Naloxone Tablet Versus Methadone for Treatment of Patients With Opioid Use Disorder (2019)

Evidence Requested for Decision-Making

- Clinical effectiveness of buprenorphine-naloxone tablets compared with methadone to treat opioid use disorder (OUD)
- Cost-effectiveness of buprenorphine-naloxone tablets compared with methadone to treat OUD
- Recommendations from evidence-based guidelines on buprenorphine-naloxone to treat OUD
- Recommendations from evidence-based guidelines on methadone to treat OUD

What We Found

- No clear patterns emerged on the comparative effectiveness of the buprenorphine-naloxone tablet and methadone for individuals with OUD
- No relevant cost-effectiveness literature was identified
- One evidence-based guideline recommends involving the patient in a discussion of their OUD treatment options
- Two evidence-based guidelines provide strong recommendations, in addition to one guideline supplement (specific to youth), for the use of buprenorphine-naloxone as treatment initiation or maintenance
- Two evidence-based guidelines focused on recommendations for pregnant people. One guideline recommends methadone first, while buprenorphine-naloxone is a suitable alternative, and switching in stable patients is not recommended unless clinically necessary. Conversely, the second guideline recommends switching people on buprenorphine-naloxone to the buprenorphine monoproduct or other alternatives

Evidence Gaps

What We Did Not Find

High-quality evidence on the comparative clinical effectiveness of the buprenorphine-naloxone tablet and methadone

Evidence comparing safety and adverse events

Evidence on cost-effectiveness

Evidence from diverse populations and settings

Canadian studies

Buprenorphine for Opioid Use Disorder During Pregnancy (2019)

Evidence Requested for Decision-Making

- Comparative clinical effectiveness of various buprenorphine formulations for the treatment of opioid use disorder (OUD) during pregnancy
- Clinical effectiveness regarding the safety of various buprenorphine formulations for the treatment of OUD during pregnancy
- Cost-effectiveness of various buprenorphine formulations for the treatment of OUD
- Recommendations from evidence-based guidelines on the use of various buprenorphine formulations for the treatment of OUD during pregnancy

What We Found

- No comparative effectiveness, safety, or cost-effectiveness literature was identified
- Two evidence-based guidelines recommend the use of buprenorphine monoproduct over buprenorphine-naloxone for the treatment of OUD during pregnancy
- One evidence-based guideline recommends the use of buprenorphine-naloxone as first-line treatment of OUD during pregnancy

Evidence Gaps

What We Did Not Find

Evidence on comparative clinical effectiveness

Evidence on safety

Evidence on cost-effectiveness

CADTH

Buprenorphine for Opioid Use Disorder (2019)

Evidence Requested for Decision-Making

- Comparative clinical effectiveness of various buprenorphine formulations for the treatment of opioid use disorder (OUD)
- Clinical evidence regarding the safety of various buprenorphine formulations for the treatment of OUD
- Cost-effectiveness of various buprenorphine formulations for the treatment of OUD
- Recommendations from evidence-based guidelines on various buprenorphine formulations for the treatment of OUD

What We Found

- No clear patterns emerged suggesting that one formulation of buprenorphine is superior to another for the treatment of OUD
- No included studies reported statistically significant differences in the safety profiles of the different buprenorphine formulations
- Two US economic evaluations were identified. One suggests that treatment of stabilized patients with OUD with implantable buprenorphine in combination with psychosocial therapy provides cost-effective benefit over generic buprenorphine in combination with psychosocial therapy. The other evaluation suggests that the buprenorphine implant in combination with psychosocial therapy does not provide cost-effective benefit compared with generic buprenorphine-naloxone in combination with psychosocial therapy
- One evidence-based guideline provides a strong recommendation for the use of buprenorphine-naloxone as first-line therapy for the treatment of OUD
- One evidence-based guideline for a military population strongly recommends considering a patient's preference between buprenorphine-naloxone or methadone when initiating treatment for OUD

Evidence Gaps

What We Did Not Find

High-quality evidence on the comparative clinical effectiveness of different buprenorphine formulations

Evidence from diverse populations

Evidence on the cost-effectiveness of different buprenorphine formulations

Canadian studies

Residential Treatment for Substance Use Disorder (2019)

Evidence Requested for Decision-Making

- Clinical effectiveness of residential treatment for individuals with substance use disorders (e.g., alcohol, drugs)

What We Found

- Limited quality evidence suggests that residential treatment may improve substance use, severity of substance use, and associated cravings
- Limited quality evidence suggests that residential treatment is equally effective or more effective than other less intensive substance use disorder treatment modalities

Evidence Gaps

What We Did Not Find

High-quality evidence on effectiveness for Indigenous populations

Telehealth-Delivered Opioid Agonist Therapy for the Treatment of Adults With Opioid Use Disorder (2018)

Evidence Requested for Decision-Making

- Clinical evidence on the use of telehealth-delivered opioid agonist therapy in patients with opioid use disorder (OUD)
- Clinical evidence on the use of home-based, self-initiated opioid agonist therapy in patients with OUD
- Cost-effectiveness of telehealth-opioid agonist therapy for patients with OUD
- Cost-effectiveness of home-based, self-initiated opioid agonist therapy for patients with OUD
- Recommendations from evidence-based guidelines on the use of telehealth or home-based opioid agonist therapy in patients with OUD

What We Found

- Limited evidence (from one non-randomized retrospective study) showed that after one year of treatment, those who participated in telehealth-delivered opioid agonist therapy were more likely to remain on uninterrupted opioid agonist therapy than those who received in-person treatment
- No clinical evidence was identified on the use of home-based, self-initiated opioid agonist therapy
- No relevant cost-effectiveness studies were identified
- One evidence-based guideline suggests that home-based, self-initiated opioid agonist therapy may be considered for patients who meet certain criteria

Evidence Gaps

What We Did Not Find

High-quality evidence on the effectiveness of telehealth-delivered opioid agonist therapy

Evidence on home-based, self-initiated opioid agonist therapy

Evidence on cost-effectiveness

Evidence specific to the adolescent population

e-Therapy Interventions for the Treatments of Substance Use Disorders and Other Addictions (2018)

Evidence Requested for Decision-Making

- Clinical effectiveness of e-therapy for the treatment of patients with substance use disorders and other addictions

What We Found

- Therapist-guided e-therapy may reduce problematic alcohol or cannabis consumption
- In one study with several limitations, therapist-guided e-therapy was equivalent to no treatment and waitlist for patients with gambling addition
- No relevant literature was identified for other substances (e.g., opioids)

Evidence Gaps

What We Did Not Find

High-quality evidence on the effectiveness of therapist-guided e-therapies

Evidence on substances other than cannabis or alcohol

CADTH

Medical Cannabis in Residential Transition or Addiction Programs (2017)

Evidence Requested for Decision-Making

- Clinical effectiveness of cannabis for adults being treated in residential transition and addiction programs
- Cost-effectiveness of cannabis for adults being treated in residential transition and addiction programs
- Recommendations from evidence-based guidelines on cannabis for adults being treated in residential transition and addiction programs

What We Found

- No relevant literature was identified

Evidence Gaps

What We Did Not Find

Evidence on clinical effectiveness

Evidence on cost-effectiveness

Recommendations from evidence-based guidelines

Concurrent Treatment for Substance Use Disorder and Trauma-Related Comorbidities (2017)

Evidence Requested for Decision-Making

- Clinical effectiveness of the concurrent treatment of substance use disorders and comorbid post-traumatic stress disorder, anxiety, or depression
- Clinical effectiveness of the treatment of one condition for the improvement of all symptoms of substance use disorder and comorbid post-traumatic stress disorder, anxiety, or depression
- Recommendations from evidence-based guidelines on how to treat substance use disorders and comorbid post-traumatic stress disorder, anxiety, or depression

What We Found

- Evidence suggests integrated treatments offer greater improvement of post-traumatic stress disorder symptoms, depression, or anxiety compared with no or minimal treatment for patients with comorbid substance use disorder
- Evidence suggests addiction-based interventions for comorbid substance use disorder and post-traumatic stress disorder were more effective at controlling substance use
- One evidence-based guideline recommended an integrated treatment approach for comorbid alcohol use disorder and post-traumatic stress disorder, or comorbid alcohol use disorder and anxiety disorder
- The same evidence-based guideline recommended cognitive behavioural therapy for comorbid alcohol use disorder and depression

Evidence Gaps

What We Did Not Find

Studies comparing treatment for post-traumatic stress disorder with treatment for substance use disorder in patients with comorbid post-traumatic stress disorder and substance use disorder

Evidence on safety and adverse events

Evidence of clinical effectiveness of treatment options over the long term

Evidence from Canadian studies

Evidence from high-quality studies (addressing the many limitations of the current body of evidence)

Buprenorphine Formulations for the Treatment of Opioid Use Disorders (2017)

Evidence Requested for Decision-Making

- Comparative clinical effectiveness of buprenorphine or buprenorphine-naloxone formulations to treat opioid use disorder
- Cost-effectiveness of buprenorphine or buprenorphine-naloxone formulations to treat opioid use disorder
- Recommendations from evidence-based guidelines on buprenorphine or buprenorphine-naloxone formulations

What We Found

- All buprenorphine formulations examined in the selected studies show a similar clinical response in patients with opioid use disorder
- Significantly higher rates of abuse, misuse, and diversion are found in sublingual buprenorphine-naloxone tablet formulations
- Buprenorphine implants are associated with high rates of treatment retention
- Rates of adverse effects were low among buprenorphine formulations, with no significant differences observed

Evidence Gaps

What We Did Not Find

Systematic reviews comparing buprenorphine formulations

High-quality, large scale randomized controlled trials comparing buprenorphine formulations

Canadian clinical or economic studies

US or Canadian evidence-based guidelines

CADTH

Buprenorphine/Naloxone Versus Methadone for the Treatment of Opioid Dependence (2016)

Evidence Requested for Decision-Making

- Clinical effectiveness of buprenorphine/naloxone compared with methadone for opioid dependence
- Cost-effectiveness of buprenorphine/naloxone compared with methadone for opioid dependence
- Recommendations from evidence-based guidelines on buprenorphine/naloxone for opioid dependence

What We Found

- Overall, buprenorphine/naloxone appears to be a safe, effective, and cost-effective choice for treating opioid use disorder compared with methadone
- More methadone patients were retained in treatment
- Buprenorphine/naloxone patients were more likely to abstain from opioid use
- Higher doses of methadone or buprenorphine/naloxone were more effective
- No statistically significant differences in harms, including mortality
- Buprenorphine/naloxone was more effective but more costly than methadone; however, in some scenarios, buprenorphine/naloxone was more effective and less costly
- One Canadian clinical practice guideline recommends that the choice of treatment be guided by clinical circumstances and patient preference

Evidence Gaps

What We Did Not Find

Evidence on longer-term treatment (more than six months)

Evidence specific to youth, younger adults, or older adults

Canadian economic analyses

Consistent use of recommended doses of the interventionand comparator in the studies

Consistent use of objective measures such as urine testing in the studies

CADTH

Rapid and Ultra-Rapid Detoxification in Adults with Opioid Addiction (2016)

Evidence Requested for Decision-Making

- Clinical effectiveness and safety of rapid opioid detoxification (ROD) and ultra-rapid opioid detoxification (UROD)
- Cost-effectiveness of ROD and UROD
- Recommendations from evidence-based guidelines on ROD and UROD

What We Found

- Some evidence suggesting earlier peaking of and lower scores for withdrawal symptoms with UROD
- Some evidence suggesting higher rates of commencement and continuation of maintenance treatment with UROD
- No significant differences between UROD and control groups in the commencement or duration of withdrawal treatment
- Mixed results in the completion of withdrawal treatment and the incidence of adverse events
- One guideline recommended against the use of UROD because of high risk for adverse events

Evidence Gaps

What We Did Not Find

Any clinical evidence on ROD

Robust, high-quality evidence on UROD

Cost-effectiveness of ROD and UROD

Crushed Buprenorphine or Buprenorphine-Naloxone for Opioid Dependency (2016)

Evidence Requested for Decision-Making

- Clinical effectiveness and safety of sublingual crushed buprenorphine for opioid dependency
- Clinical effectiveness and safety of sublingual crushed buprenorphine-naloxone for opioid dependency
- Recommendations from evidence-based guidelines on the administration of crushed buprenorphine or crushed buprenorphine-naloxone

What We Found

- No statistically significant differences in opioid withdrawal or opioid craving between the whole buprenorphine tablet or the crushed tablet
- Number of patients experiencing adverse events was higher in the crushed tablet group; however, there were no serious adverse events reported in either group

Evidence Gaps

What We Did Not Find

Evidence on the effectiveness of crushed tablets in resolving misuse and diversion issues

Relevant studies comparing sublingual administration of crushed buprenorphine-naloxone with uncrushed buprenorphine or uncrushed buprenorphine-naloxone tablets or buprenorphine-naloxone film for the treatment of opioid dependency

Evidence-based guidelines on the use of crushed buprenorphine or crushed buprenorphine-naloxone

CADTH

Occupational Therapy Interventions to Prevent Opioid Relapse (2016)

Evidence Requested for Decision-Making

- Clinical effectiveness of occupational therapy to prevent relapse of opioid use in patients with chronic pain or opioid dependence
- Cost-effectiveness of occupational therapy to prevent relapse of opioid use in patients with chronic pain or opioid dependence
- Recommendations from evidence-based guidelines on occupational therapy to prevent relapse of opioid use

What We Found

- No relevant literature was identified

Evidence Gaps

What We Did Not Find

Evidence on clinical effectiveness

Evidence on cost-effectiveness

Recommendations from evidence-based guidelines

Yoga for the Treatment of Post-Traumatic Stress Disorder, Generalized Anxiety Disorder, Depression, and Substance Use (2015)

Evidence Requested for Decision-Making

- Clinical effectiveness of yoga to treat substance use disorder
- Recommendations from evidence-based guidelines on yoga to treat substance use disorder

What We Found

- Evidence suggesting yoga may help some symptoms in adults with substance use and addiction

Evidence Gaps

What We Did Not Find

High-quality evidence on the clinical effectiveness and safety of yoga over the long term for substance use and addiction

Evidence for diverse populations with substance use and addiction

Recommendations from evidence-based guidelines

CADTH

Mindfulness Interventions for the Treatment of Post-Traumatic Stress Disorder, Generalized Anxiety Disorder, Depression, and Substance Use Disorders (2015)

Evidence Requested for Decision-Making

- Clinical effectiveness of mindfulness interventions to treat substance use disorder
- Recommendations from evidence-based guidelines on mindfulness to treat substance use disorder

What We Found

- One low-quality, randomized controlled trial suggests that mindfulness is more effective than "treatment as usual" in lowering the risk of relapse to substance use and heavy drinking
- One evidence-based guideline suggests that mindfulness can be used by suitably trained and experienced professionals to treat patients with problematic drug and alcohol use

Evidence Gaps

What We Did Not Find

High-quality evidence from studies with larger sample sizes

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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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