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CADTH RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

Telehealth-Delivered Opioid Agonist Therapy for the Treatment of Adults with Opioid Use Disorder: Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines

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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, medical devices, diagnostics, and procedures in our health care system.

Context and Policy Issues

The misuse of opioids (such as heroin, oxycodone, hydromorphone and fentanyl) has been an increasingly common health concern in Canada and the United States. The number of individuals enrolled in opioid use-related medical treatment programs in Ontario increased from 6,000 to over 40,000 from the years 2000 to 2016, with 865 opioid-related deaths reported in Ontario in 2016.[1] One way with which opioid use disorder can be managed is with opioid agonist therapy (OAT) which is part of a harm reduction strategy of care and includes methadone, or buprenorphine/naltrexone, often delivered alongside non-pharmacological therapy such as counselling.[2,3] In Canada, access to OAT remains a challenge in many parts of the country, particularly in rural and remote areas because of the increased demand for treatment, and is associated with extensive waiting periods with significant health and financial burdens.[4] Telehealth-delivered OAT for substance use disorders was developed with the aim to alleviate this demand/capacity issue.[5,6] Usually, telehealth-delivered OAT can happen with the patient presenting at a videoconference site, usually located at a clinic under the supervision of a registered nurse, where they can be connected to a physician in a different location, or can be home-based where patients can initiate the treatment without supervision.

This Rapid Response report aims to review the effectiveness of the use of telehealth-delivered OAT compared to standard OAT. Cost-effectiveness and evidence-based guidelines regarding the use of telehealth-delivered OAT for the treatment of opioid use disorders will also be examined.

Research Questions

1. What is the clinical evidence regarding the use of telehealth-delivered opioid agonist therapy (alone or in combination with other approaches) in patients with opioid use disorder?
2. What is the clinical evidence regarding the use of home-based, self-initiated opioid agonist therapy in patients with opioid use disorder?
3. What is the cost-effectiveness of telehealth-opioid agonist therapy for patients with opioid use disorder?
4. What is the cost-effectiveness of home based, self-initiated opioid agonist therapy for patients with opioid use disorder?
5. What are the evidence-based guidelines regarding the use of telehealth or home-based opioid agonist therapy in patients with opioid use disorder?

Key Findings

Limited evidence from one non-randomized retrospective study showed that after one year of treatment, those who participated in telehealth-delivered OAT were more likely to remain on uninterrupted OAT than those who received in-person OAT.

The British Columbia Centre of Substance Abuse recommends that home-based, self-initiated OAT may be considered for those who have previous experience with OAT, or who have significant barriers to office attendance, while those who express significant apprehension of experiencing withdrawal, or those with concurrent alcohol and sedative use or misuse, are not likely to be good candidates for home induction.

No relevant clinical studies regarding the use of home-based self-initiated therapy and no relevant cost-effectiveness studies regarding the use of telehealth or home-based self-initiated OAT were identified.

Methods

A limited literature search was conducted on key resources including PubMed, CINAHL, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No methodological filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2013 and September 6, 2018.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adolescents (ages 12 to 17) and adults (≥18 years) with opioid use disorder
Intervention	Q1 & Q3: Combined telehealth and opioid agonist therapy (OAT) Q2 & Q4: Home-based OAT Q5: Evidence-based guidelines
Comparator	Q1 & Q3: Standard care for OAT (office-based care, clinic based care), other OAT delivery models (including home-based OAT) Q2 & Q4: Standard care for OAT (office-based care, clinic based care), other OAT delivery models (including telehealth OAT) Q5: No comparator
Outcomes	Q1 & Q2: Effectiveness (e.g., reduced overdose; retention; compliance, Safety [patient harms and benefits]) Q3 & Q4: Cost-effectiveness (e.g., cost per hospitalization avoided, cost per overdose avoided, cost per QALY increase) Q5: Guidelines
Study Designs	Heath technology assessments (HTAs), systematic reviews (SRs) and meta-analyses (MAs), randomized controlled trials (RCTs), non-RCTs, economic evaluations, guidelines

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2013.

Critical Appraisal of Individual Studies

The included clinical study was critically appraised using the Downs and Black,[7] and AGREE II[8] checklists, respectively. A summary score was not calculated for the included study; rather, a review of the strengths and limitations was described.

Summary of Evidence

Quantity of Research Available

A total of 243 citations were identified in the literature search. Following screening of titles and abstracts, 235 citations were excluded and eight potentially relevant reports from the electronic search were retrieved for full-text review. One potentially relevant publication was retrieved from the grey literature search. Of these potentially relevant articles, seven publications were excluded for various reasons, while two publications met the inclusion criteria and were included in this report. Appendix 1 presents the PRISMA flowchart of the study selection.

Summary of Study Characteristics

A detailed summary of the included studies is provided in Appendix 2.

The report included one clinical study[9] and one evidence-based guideline.[10]

The clinical study is a non-randomized observational cohort study that compared telemedicine-delivered OAT to in-person OAT.[9] Participants (median age = 31 years) received methadone or buprenorphine and were divided into three groups by physician interactions: predominantly telemedicine OAT (<75% telemedicine OAT; n – 1,590), predominantly in-person OAT (<25% telemedicine OAT; n = 1,745) and mixed treatment group (≥25% and ≤75% telemedicine OAT; n = 418). Outcomes reported were one-year retention rates (rates of patients who received continuous and uninterrupted OAT for one year). The study was conducted in Canada.

The included guideline is a British Columbia Ministry of Health evidence-based guideline for the clinical management of adults with opioid use disorder.[10] Guideline content and recommendations were based on a structured review of the literature (details not reported).The evidence and recommendation rating were adopted from the classification developed by the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) workgroup.

Summary of Critical Appraisal

Details of the strengths and limitations of the included study are summarized in Appendix 3.

The included study[9] was a non-randomized retrospective cohort study, the hypotheses were clearly described, the method of selection from the source population and representation were described, losses to follow-up were reported, main outcomes, interventions, patient characteristics, and main findings were clearly described, and estimates of random variability and actual probability values were provided. The study did

not perform calculations to determine that it was powered to detect a clinically important effect. The study did not have a group with pure intervention: all three groups had overlapping therapies. This non-pure intervention grouping and the non-randomized retrospective design limited its internal validity as the patients may have preferentially selected their treatment options thus biasing the retention rate outcome. The study had a good external validity based on the included population of patients with opioid substance disorder.

The included guideline[10] had a clear scope and purpose, the recommendations are specific and unambiguous, methods used for formulating the recommendations were clearly described, health benefits, side effects and risks were stated in the recommendations, and the procedures for updating the guidelines provided and target users of the guideline are clearly defined. The methods for searching for and selecting the evidence were unclear. The potential cost implications of applying the recommendation were not included. It was unclear whether the guideline was piloted among target users, or whether patients' views and preferences were sought.

Summary of Findings

Clinical Effectiveness of Telehealth Delivered Opioid Agonist Therapy

The non-randomized study compared predominantly telehealth-delivered OAT to predominantly in-person OAT and mixed treatment.[9] Patients with telehealth-delivered OAT had a retention rate of 50% at one year of treatment compared to 39% for patients with in-person OAT. Those receiving telehealth treatment were 1.27 times more likely to continue OAT treatment without interruption for one year than were those attending in-person OAT. The retention rate for the mixed treatment group was 47% at one year and those receiving mixed treatment were 1.26 times more likely to continue treatment than patients with in-person OAT. The authors concluded that telehealth-delivered OAT may be an effective alternative to in-person OAT, especially in rural and remote regions. Further detail is provided in Appendix 4.

Clinical Effectiveness of Home-based, Self-initiated Opioid Agonist Therapy

There were no relevant studies regarding the clinical evidence of home-based, self-initiated OAT for patients with opioid use disorder identified.

Cost-Effectiveness of Telehealth Delivered Opioid Agonist Therapy

There were no relevant cost-effectiveness studies regarding the use of telehealth-delivered OAT for patients with opioid use disorder identified.

Cost-Effectiveness of Home Based, Self-Initiated Opioid Agonist Therapy

There were no relevant cost-effectiveness studies regarding home-based OAT for patients with opioid use disorder identified.

Guidelines Regarding the use of Telehealth or Home-Based Opioid Agonist Therapy

The British Columbia Centre for Substance Abuse produced guidelines for the clinical management of adults with opioid use disorder.10 Regarding the use of home-based, self-initiated OAT, the guidelines recommend that patients who have previous experience with buprenorphine/naloxone treatment and have a stable home environment may be

candidates for home-based induction of treatment, especially those who have barriers to in-person attendance such as work, school, and child care. On the other hand, they state that patients who have a significant fear regarding withdrawal and concurrent alcohol and sedative use or misuse may not be good candidates for home-based OAT induction unless they can be monitored by a caregiver.

Details of findings are summarized in Appendix 4.

Limitations

Findings from the included clinical study was limited to patients retention rate outcome, and should be interpreted with caution based on the nature of a non-randomized retrospective design which are prone to selection and recall bias. The treatment groups with overlapping treatment strategies made the comparison between groups not pure, and may affect the internal validity of the findings. Additionally, while the non-randomized study did include participants who were 15 years and older, those who were younger than 18 accounted for less than 1% of the cohort and thus it is unclear whether the results generalize to the adolescent population. There was no evidence found on the clinical effectiveness of home-based, self-initiated OA, nor the cost-effectiveness of telehealth or in-person OAT.

Conclusions and Implications for Decision or Policy Making

Limited evidence, based on one non-randomized study, showed that telehealth-delivered OAT seemed to be associated with a higher likelihood of uninterrupted treatment retention at one year than in-person OAT. The British Columbia Centre of Substance Abuse recommends that home-based, self-initiated OAT may be considered for patients who have previous experience with OAT, or who have significant barriers to office attendance, while patients who express significant apprehension of experiencing withdrawal, or those with concurrent alcohol and sedative use or misuse, are not likely to be good candidates for home induction.

While the included study did not examine effectiveness outcomes other than treatment retention, an open label randomized controlled trial, which is not included in this review because of its irrelevant comparator, compared the effectiveness of take-home self-administered OAT treatment to waiting list over a 12-week period for participants with heroin dependence.[11] After 12-weeks, heroin use by those in the treatment group heroin was on average 19.02 days less per month compared to those on the wait-list.

It is uncertain as to whether telehealth-delivered OAT is as clinically effective as standard, in-person therapy. Large RCTs on the clinical effectiveness of telehealth or home-based OAT compared to in-person OAT would reduce the uncertainty. Cost-effectiveness studies on the use of telehealth or home-based OAT in a Canadian context are needed for decision makers to weigh benefits and costs of OAT for Canadians with opioid use disorders.

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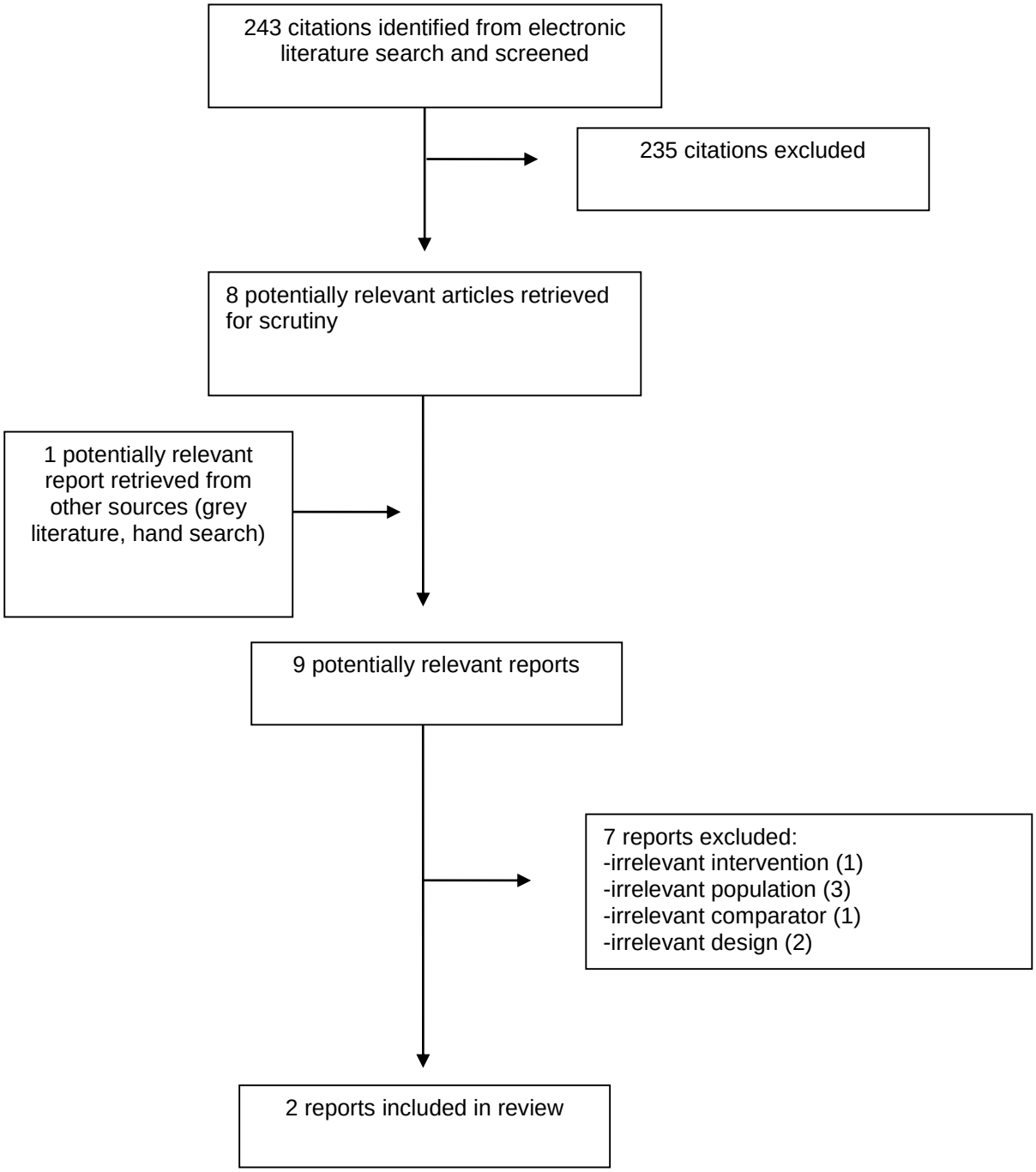
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Clinical Study

First author, year, country	Study design, objectives	Intervention Comparators	Population	Main study outcomes
Eibl,[9] 2017, Canada	Non-RCT retrospective cohort study *"This study compared treatment outcomes for in-person versus telemedicine-delivered OAT"* (p 133)	Telemedicine-delivered OAT In-person OAT	Patients (aged 15 years and older) with opioid use disorder Predominantly in-person OAT (<25% telemedicine): n = 1,745 Predominantly telemedicine OAT (>75% telemedicine): n = 1,590 Mixed OAT (≥25% and ≤75% telemedicine): n = 418 Patients started on methadone or buprenorphine and were allowed to transition between these medications over the course of treatment	Retention rate (Medication discontinuation was defined as 30 continuous days without a methadone or buprenorphine dose. A patient defined as having been retained in treatment if they completed at least one year of continuous and uninterrupted OAT)

OAT = opioid agonist therapy; RCT = randomized controlled trial

Table 3: Characteristics of Included Guidelines

Group, Year	Scope	Population	Evidence	Grading system
British Columbia Ministry of Health Guidelines,[10] 2017	Guideline for the clinical management of opioids use disorders	Adults with opioids use disorders	Systematic structured evidence review done by the British Columbia Centre on Substance Use (BCCSU) (literature search period unclear; database searched not reported)	The evidence and recommendation rating were adopted from the classification developed by the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) workgroup. The GRADE system primarily involves consideration of the following factors: overall study quality (or overall risk of bias or study limitations), consistency of evidence, directness of evidence, and precision of evidence.

Appendix 3: Critical Appraisal of Included Publications

Table 4: Strengths and Limitations of Included Clinical Studies(Downs and Black[7])

Strengths	Limitations
Eibl, 2017[9]	
• hypothesis clearly described • method of selection from source population and representation described • loss to follow-up reported • main outcomes, interventions, patient characteristics, and main findings clearly described • estimates of random variability and actual probability values provided	• patients not randomized • there is no group with pure intervention • unclear whether study had sufficient power to detect a clinically important effect

Table 5: Strengths and Limitations of Included Guidelines (AGREE II[8])

Strengths	Limitations
British of Columbia Ministry of Health Guidelines, 2017[10]	
• scope and purpose of the guidelines are clear • the recommendations are specific and unambiguous • the method for searching for and selecting the evidence are clear • methods used for formulating the recommendations are clearly described • health benefits, side effects and risks were stated in the recommendations • procedure for updating the guidelines provided • target users of the guideline are clearly defined	• unclear whether the guideline was piloted among target users • unclear whether patients' views and preferences were sought • potential cost implications of applying the recommendation not included

Appendix 4: Main Study Findings and Author's Conclusions

Table 6: Summary of Findings of Included Studies

Main Study Findings	Author's Conclusion
Eibl, 2017[9] (Non-Randomized Study)	
Retention rate (% at one year; aOR) *Telemedicine OAT* (n = 1,590): patients more likely to be retained in therapy than patients treated in-person aOR= 1.27; 95% CI 1.14–1.41; *P* < 0.001 Retention rate at one year: 50% *In-person* OAT (n = 1,745) Retention rate at 1 year: 39% *Mixed group* (n = 418) also had higher likelihood of retention than the in-person group aOR=1.26; 95% CI 1.08–1.47; *P* = 0.001 Retention rate at 1 year: 47%	*"Telemedicine may be an effective alternative to delivering in person OAT, and it has the potential to expand access to care in rural, remote, and urban regions"* (p 133)

aOR = odd ratio adjusted for age, sex, clinic region, clinic rurality, and peak methadone dose; OAT = opioid agonist therapy

Table 7: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
British Columbia Ministry of Health Guidelines, 2017[10]	
". Patients that have previous experience with buprenorphine/naloxone treatment, demonstrated reliability, a sufficiently stable home environment and ability to store medication safely may be good candidates for home induction. *. Patients with significant barriers to office attendance (e.g., work, school, child-care) and/or retention in care who meet the preceding criteria, or who have a caregiver that does, may also be considered.* *. Patients who express significant apprehension or fear of experiencing withdrawal, or those with concurrent alcohol and sedative use or misuse, are not likely to be good candidates for home induction, unless adequate monitoring can be provided from a responsible caregiver.* *. Prior to home induction, discussion of risks and benefits of home induction must be documented and informed consent secured from the patient.* *. During home induction, clinicians should be willing and able to provide regular follow-up and support via telephone. All such contact should be documented in the patient's chart. It is recommended that patients be seen in-person within 2 days of home induction. Patients with previous experience taking buprenorphine/naloxone may require less intensive support.• . Patients should be provided with clinic/office contact information, in-person education and written instructions for dosing and*	Not reported

Recommendations	Strength of Evidence and Recommendations
timing, including use of the Subjective Opioid With-drawal Scale (SOWS, see Appendix 7) to assess withdrawal symptoms and determine when to start induction (SOWS score ≥ 17), if appropriate. *. Patients and/or caregivers should be instructed to contact the office immediately in the event of any problems and be willing to come in for clinical assessment as required." (p 44)* Take-home Dosing Recommendations and Strategies to Reduce Diversion for Oral Agonist Therapy *"Take-home dosing of oral agonist therapy may be beneficial in terms of improved motivation to participate in agonist treatment, improved treatment retention, increased patient autonomy and flexibility, positive reinforcement of abstinence, decreased treatment burden, and decreased costs related to daily witnessed ingestion. However, these benefits must be balanced against patient and public health risks associated with take-home dosing"* (Appendix 4, p 53 – 56)	