McMaster University | HEALTH FORUM

Rapid Evidence Profile

Examining the effects of care models and program elements of repeat treatment approaches for substance use and concurrent mental health conditions

12 February 2023

[MHF product code: REP 62]

Appendix 1: Methodological details

We use a standard protocol for preparing rapid evidence profiles (REP) to ensure that our approach to identifying research evidence is as systematic and transparent as possible in the time we were given to prepare the profile.

Identifying research evidence

For this REP, we searched Health Systems Evidence, the Cochrane Database of Systematic Reviews, PubMed and PsychInfo for:
1) evidence syntheses
2) protocols for evidence syntheses that are underway
3) single studies.

For Health Systems Evidence, we used a filter for 'mental health and addictions' combined with an open text search for repeat OR resistant OR refractory OR recalcitrant. We searched Cochrane Database of Systematic Reviews using the MESH major subject heading of 'Substance-related disorder.' We searched PubMed using an open-text search for ((substance use disorder) OR (drug misuse) OR (addiction) OR (drug abuse) OR (substance use) OR (substance dependence)) OR (Substance-Related Disorders[MeSH Major Topic]) OR (Substance-Related Disorders[MeSH Terms])) AND (treatment OR model) AND (repeat OR resistant OR refractory OR recalcitrant) combined with filters for Systematic Review and the last 10 years. Links provide access to the full search strategy. We searched PsychInfo using an open-text search for ((substance use disorder) OR (drug misuse) OR (addiction) OR (drug abuse) OR (substance use) OR (substance dependence)) OR (Substance-Related Disorders[MeSH Major Topic]) OR (Substance-Related Disorders[MeSH Terms])) AND (treatment OR model) AND (repeat OR resistant OR refractory OR recalcitrant) combined with filters for the last 10 years.

Additional searches were completed following feedback from requestors in PubMed focused on residential treatment (or inpatient treatment) and alcohol use disorder. For the residential treatment search, we used an open-text search for (substance use disorder) AND (inpatient OR residential) AND (treatment), with filters applied for systematic reviews and for the last five years. For the alcohol use disorder search, we used an open-text search for (alcohol use disorder) AND (inpatient OR residential OR outpatient) AND (treatment), with filters applied for systematic reviews.

Each source for these documents is assigned to one team member who conducts hand searches (when a source contains a smaller number of documents) or keyword searches to identify potentially relevant documents. A final inclusion assessment is performed both by the person who did the initial screening and the lead author of the rapid evidence profile, with disagreements resolved by consensus or with the input of a third reviewer on the team. The team uses a dedicated virtual channel to discuss and iteratively refine inclusion/exclusion criteria throughout the process, which provides a running list of considerations that all members can consult during the first stages of assessment.

During this process we include published, pre-print and grey literature. We do not exclude documents based on the language of a document. However, we are not able to extract key findings from documents that are written in languages other than Chinese, English, French or Spanish. We provide any documents that do not have content available in these languages in an appendix containing documents excluded at the final stages of reviewing. We excluded documents that did not directly address the research questions and the relevant organizing framework.

Assessing relevance and quality of evidence

We assess the relevance of each included evidence document as being of high, moderate or low relevance to the question.

Two reviewers independently appraised the quality of the guidelines we identified as being highly relevant using AGREE II. We used three domains in the tool (stakeholder involvement, rigour of development and editorial independence) and classified guidelines as high quality if they were scored as 60% or higher across each of these domains.

Two reviewers independently appraise the methodological quality of evidence syntheses that are deemed to be highly relevant. Disagreements are resolved by consensus with a third reviewer if needed. AMSTAR rates overall methodological quality on a scale of 0 to 11, where 11/11 represents an evidence synthesis of the highest quality. High-quality evidence syntheses are those with scores of eight or higher out of a possible 11, medium-quality evidence syntheses are those with scores between four and seven, and low-quality evidence syntheses are those with scores less than four. It is important to note that the AMSTAR tool was developed to assess evidence syntheses focused on clinical interventions, so not all criteria apply to those pertaining to health-system arrangements or to economic and social responses. Where the denominator is not 11, an aspect of the tool was considered not relevant by the raters. In comparing ratings, it is therefore important to keep both parts of the score (i.e., the numerator and denominator) in mind. For example, an evidence synthesis that scores 8/8 is generally of comparable quality to another scoring 11/11; both ratings are considered 'high scores.' A high score signals that readers of the evidence synthesis can have a high level of confidence in its findings. A low score, on the other hand, does not mean that the evidence synthesis should be discarded, merely that less confidence can be placed in its findings and that the evidence synthesis needs to be examined closely to identify its limitations. (Lewin S, Oxman AD, Lavis JN, Fretheim A. SUPPORT Tools for evidence-informed health Policymaking (STP): 8. Deciding how much confidence to place in a systematic review. *Health Research Policy and Systems* 2009; 7 (Suppl1): S8.)

Identifying experiences from other countries and from Canadian provinces and territories

For each REP, we work with the requestors to collectively decide on what countries (and/or states or provinces) to examine based on the question posed. For other countries, we search relevant government and stakeholder websites including websites of ministries and departments responsible for Veterans Affairs and those responsible for providing health insurance for Veterans. In Canada, a similar approach was used, searching the website of Veterans Affairs Canada and reviewing the health benefits grid. While we do not exclude content based on language. Where information is not available in English, Chinese, French or Spanish, we attempt to use site-specific translation functions or Google translate. A full list of websites and organizations searched is available upon request.

Preparing the profile

Each included document is cited in the reference list at the end of the REP. For all included guidelines, evidence syntheses and single studies (when included), we prepare a small number of bullet points that provide a summary of the key findings, which are used to summarize key messages in the text. Protocols and titles/questions have their titles hyperlinked, given that findings are not yet available.

We then draft a summary that highlights the key findings from all highly relevant documents (alongside their date of last search and methodological quality) as well as key findings from the jurisdictional scan.

Appendix 2: Summary of key findings from highly relevant evidence documents on the effects of models of care for repeat substance-use treatment on equity-centred quadruple-aim outcomes

Types of substance and program elements	Multiple substances	Alcohol	Opioids
Psychotherapy		*Health outcomes* • One recent high-quality evidence synthesis found alcoholics anonymous and 12-step facilitation are more effective than other clinical interventions for abstinence and led to substantial healthcare cost savings among people with alcohol use disorder (1) • One recent low-quality evidence synthesis found dialectic behavioural therapy reduced alcohol consumption among individuals with combined alcohol use disorder and borderline personality disorder (2) • One small single study reported in a recent high-quality evidence synthesis found positive results for motivational interviewing and alcohol abstinence (3) • One recent single study found unilateral family therapy to be effective in facilitating treatment entry, drinking reduction and long-term improvement in psychological health and marital functioning among treatment-resistant alcohol-using individuals (4) *Patient experience* • One recent medium-quality evidence synthesis found psychosocial interventions compared to medication-based interventions were more likely to demonstrate improved treatment engagement and recovery (5)	*Health outcomes* • One recent single study found providing adjunctive personalized psychosocial interventions (including psychological change methods such as contingency management and recovery activities) alongside standard opioid agonist therapy was more effective in helping treatment-resistant patients than standard medication-assisted therapies (6) • One recent high-quality evidence synthesis found no evidence to support the use of one psychosocial treatment over another to reduce the use of substances or improve the mental health of those with chronic opioid or substance use (3) • One older high-quality evidence synthesis found very limited evidence to support any specific approach to facilitate benzodiazepine discontinuation among chronic benzodiazepine users *Care experience* • One older low-quality evidence synthesis found contingency management showed promise to increase retention in medication-assisted therapy for treatment-refractory individuals who use opioids (7) • One recent medium-quality evidence synthesis found that integrating shared decision-making and providing treatment options for people with opioid use disorder was beneficial and improved retention to treatment and satisfaction with care (8) *Costs* • One recent single study found combining adjunctive personalized psychosocial interventions with standard medication-assisted therapies for those with treatment-resistant opioid use had a 60–67% probability of being cost effective (at a willingness-to-pay threshold of £20,000 to 30,000 per quality-adjusted life year) (6)
Medication		*Health outcomes* • Two recent medium-quality evidence synthesis found mixed effects of ketamine for individuals with alcohol use disorder who fail to respond to first-line agents, with one	*Health outcomes* • One recent medium-quality evidence synthesis found supervised consumption of oral heroin (diacetylmorphine) may be effective for treating individuals with treatment-refractory heroin-dependence (15)

Types of substance and program elements	Multiple substances	Alcohol	Opioids
		suggesting it is effective in reducing cravings and alcohol consumption, while the other was unable to report definitive conclusions (9; 10) • One recent high-quality evidence synthesis found acamprosate, topiramate and oral naltrexone reduced alcohol consumption among people with alcohol use disorder (11) o However, a recent medium-quality evidence synthesis found insufficient evidence to support the initiation of naltrexone in the emergency department or inpatient setting for the management (12) • One recent high-quality evidence synthesis found insufficient evidence to support the use of gabapentin for inpatients with acute alcohol withdrawal syndrome (13) *Care experience* • One recent medium-quality evidence synthesis found perceived barriers to obtaining community-based pharmacotherapy for alcohol use disorder includes lack of knowledge about services, complexity of prescribing, treatment philosophy and stigma, and medication accessibility including formulary restrictions (14)	• One recent medium-quality review found oral diacetylmorphine may be effective as a maintenance treatment for treatment-refractory heroin-dependent individuals that have never injected heroin • One older single study reported no significant differences in health outcomes between supervised injectable heroin treatment, supervised injectable methadone treatment or oral methadone treatment for chronic-opioid users, but street heroin use had a greater decline among those using injections as compared to those consuming methadone orally (16) • One recent single study found extended-release buprenorphine resulted in improved retention as well as a reduction in emergency department visits, reduction in illicit opioid, and homelessness among Veterans with chronic-opioid use disorder (17) *Care experience* • One older medium-quality review and one older low-quality evidence synthesis found heroin-assisted treatment to have greater retention rates among treatment-refractory individuals compared to either naltrexone, buprenorphine or methadone (7; 18) o The older medium-quality evidence synthesis noted a significantly higher rate of adverse events from supervised injection of heroin as compared to oral methadone maintenance therapy (18) o The older low-quality evidence synthesis found improved retention from methadone compared to buprenorphine, particularly when buprenorphine was delivered flexibly or at low-fixed doses (7) • One older single study found diacetylemorphine was found to be more effective in retaining people with opioid-dependence refractory to treatment than methadone maintenance therapy (19) • One older single study found high-threshold, high-dose methadone programs to improve retention among individuals with treatment-resistant opioid-use and comorbid bipolar disorder (20) *Costs* • One older single study found diacetylemorphine may be more cost-effective than methadone maintenance therapy among those with opioid-dependence refractory to treatment (19)

Types of substance and program elements	Multiple substances	Alcohol	Opioids
Other (including combined therapies)	*Health outcomes* • One recent medium-quality evidence synthesis found positive effects for integrated treatment models including both pharmacologic and psychologic treatment for those with comorbid mental illness and substance dependence (21) • Two medium-quality evidence syntheses found residential treatment to be largely effective for those with substance-use disorder (21; 22) o Core components of residential treatment included withdrawal and medication management, psychological treatment (motivational interviewing, CBT and mindfulness-based techniques) as well as auxiliary services including spiritual guidance and a range of social, employment and sexual health services (21) • One medium-quality evidence synthesis found both residential and non-residential treatment programs improved rates of abstinence among Indigenous participants when they included culturally appropriate care (23) o Elements of culturally appropriate care included sweat lodge ceremonies, smudging, drumming and healing circles as well as traditional activities of fishing and hunting o Common treatment models in residential treatment include detoxification, 12-step abstinence, dialectical behavioural therapy, land-based culture camps and culture as treatment	*Health outcomes* • One recent medium-quality evidence synthesis found combined naltrexone and psychosocial interventions improved heavy drinking, but was less effective for patients with concurrent mental health conditions (26) *Costs* • One recent single study found a $68 per month savings from providing a navigator-based intervention for repeat Medicaid visitors at a detox centre (27)	*Health outcomes* • Two recent medium-quality evidence synthesis and one recent single study (based on a single case) found that based on a very small number of case reports, deep brain stimulation may be effective in reducing the consumption of illicit drugs for treatment-refractory opioid users (28-30) o However, some adverse events were reported including dizziness, insomnia and weight gain, as well as an increase in substance use among three participants • One recent low-quality evidence synthesis found non-invasive brain stimulation reduced the effects of withdrawal, detoxification and cravings for individuals with chronic opioid use (31) • One recent single study found long-term involuntary treatment that emphasizes independence, where possible, and draws on a wide range of disciplines and treatment approaches including psychotherapy and medication can be effective at improving psychiatric symptoms, self-care behaviour, verbal skills and disability among subsets of treatment-resistant dual-diagnosis individuals (32)

Types of substance and program elements	Multiple substances	Alcohol	Opioids
	○ Non-residential treatment included community-based programming, 12-step programs, talking circles, pharmacotherapy or substitution therapy, behavioural support groups and group therapy (23) *Patient experience* • One recent medium-quality evidence synthesis found inconclusive results related to post-discharge supports for patients existing inpatient care to outpatient community-based care ○ Facilitators for successful transitions included leveraging existing partnership between organizations, building trust and continuity across settings, and keeping open lines of communication (24) • One recent medium-quality evidence synthesis found contexts influenced the effectiveness of treatment for substance-use disorder ○ The evidence synthesis identified that clients entering residential treatment had comparably better outcomes when they had previous involvement in the justice system, had a high severity of substance use, and had positive pre-treatment relationships with friends and family (25)		

Appendix 3: Detailed data extractions from evidence syntheses about models of care for repeat substance-use treatment

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations

• Types of substance(s) used
  ○ Opioids
• Program elements used in repeat treatment
  ○ Psychotherapy
  ○ Medication
• Where are repeat treatments provided
  ○ Outpatient
• Outcomes
  ○ Care experience
	Heroin-assisted treatment was associated with better retention than methadone among treatment-refractory patients (7)
	• Identified factors associated with the outcome of retention in medication-assisted treatment for opiate-dependence
	• Retention in treatment was found to decrease as duration of follow-up lengthens
	• With regards to medication, the review found that patients in randomized controlled trials who received naltrexone or buprenorphine had better three-, six- and 12-month retention than those who received a placebo or no medication
	• Studies found that patients who received methadone rather than buprenorphine/naloxone were more likely to be retained and four- and six-month follow-up
	  ○ Buprenorphine had significantly lower retention when delivered flexibly or at low fixed doses
	• Studies also found benefits to retention of heroin-assisted treatment relative to oral methadone among treatment-refractory patients
	• Only contingency management showed promise as a behavioural therapy intervention to increase retention in medication-assisted therapy for opiate dependence
		High	No	3/9	2016	No	Not reported

• Types of substance(s) used ○ Alcohol • Eligibility for repeat treatments	Protocolized escalation of benzodiazepines as an alternative to a symptom-triggered approach may decrease	Medium	No	3/9	2015	No	Not reported

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
○ Clinician referral or approval • Program elements used in repeat treatments ○ Medication • Outpatient ○ Health outcomes	the need for mechanical ventilation and intensive care among patients experiencing severe, refractory alcohol withdrawal (33) • The review also found that propofol is appropriate for patient refractory to benzodiazepines						
• Types of substance(s) used ○ Opioid ▪ Heroin • Eligibility for repeat treatments ○ Clinician referral or approval • Program elements used in repeat treatments ○ Medication • Where are repeat treatments provided ▪ Outpatient • Outpatient ○ Health outcomes ○ Care experience	Oral diacetylmorphine may be effective only for treatment-refractory patients with heroin dependence as maintenance treatment for those who have never injected or inhaled opioids, as maintenance for those who want to switch from injection to oral administration, and to reduce opioid withdrawal symptoms (15)	High	No	6/10	2020	No	None reported
• Types of substance(s) used ○ Alcohol ○ Opioid ▪ Heroin • Eligibility for repeat treatments ○ Time since last treatment for substance use ○ Clinician referral or approval • Program elements used in repeat treatments ○ Other (deep brain stimulation) • Where are repeat treatments provided ○ Outpatient • Priority population ○ People who have been previously admitted to inpatient treatment programs • Outpatient ○ Health outcomes ○ Care experience	Based on a very small sample, deep brain stimulation may offer treatment for refractory patients who are at risk of mortality (28) • The review examines the effectiveness of deep brain stimulation through the nucleus accumbens, while transcranial magnetic stimulation is another form of stimulation that is not permanently implanted • The review presents previously reported cases of deep brain stimulation for substance-use disorder • The review included 13 case reports, which included 33 patients • All included case reports required that patients were diagnosed with substance-use disorder according to the DSM and were refractory to multiple other therapies and had	High	No	4/10	2020	No	Not reported

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
	several years of drug abuse with a minimum of three years • Remission rates at six months and at one year were 61% and 53% respectively, and for those studies that followed patients for more than two years remission rate was 43% • All studies documented a reduction in substance use in at least one of their patients, with eight studies reporting a reducing in cravings and seven reporting an improvement in quality of life • Eight studies reporting adverse effects included dizziness, insomnia and weight change, while three patients reported increase in substance use during treatment						

• Types of substance(s) used
  ○ Opioid
  ▪ Heroin
• Eligibility for repeat treatments
  ○ Time since last treatment for substance use
  ○ Clinician referral or approval
• Program elements used in repeat treatments
  ○ Medication
• Where are repeat treatments provided
  ○ Outpatient
• Priority population
  ○ People who have been previously admitted to inpatient treatment programs
• Outpatient
  ○ Health outcomes
  ○ Care experiences
	For individuals with treatment resistant opioid-use dependence supervised injection of heroin may offer an effective treatment, but this potential must be weighed against reported side effects (18)
	• Supervised -injection heroin is not a first-line treatment but an option for patients who have not responded to standard treatment including oral methadone maintenance treatment or residential rehabilitation
	• Injectable doses are typically between 150–250 mg per injection and are taken under direct medical or nursing supervision ensuring safety and possible diversion, but this model is quite expensive and requires a high level of support
	• In all included studies, a positive effect on illicit heroin use was reported and there was a significant advantage in retention when compared to oral methadone maintenance therapy
		High	No	7/11	Published in 2015	No	Not reported

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
	• However, the studies showed a significantly higher risk of side effects compared with oral methadone maintenance therapy treatment groups						

• Types of substance(s) used
  ○ Opioid
  ▪ Heroin
• Eligibility for repeat treatments
  ○ Time since last treatment for substance use
  ○ Clinician referral or approval
• Program elements used in repeat treatments
  ○ Medication
• Where are repeat treatments provided
  ○ Outpatient
• Priority population
  ○ People who have been previously admitted to inpatient treatment programs
• Outpatient
  ○ Health outcome
  ○ Care experiences
	No significant evidence supports the use of one psychosocial treatment to reduce substance use or improve mental state for people with severe mental illnesses over another (3)
	• One small study reported positive results for motivational interviewing and alcohol abstinence
	• It should be noted that these findings do not mean that particular treatments do not help but that there is little supportive evidence to suggest one form of support should be taken over another
		High	No	11/11	2018	No	Not reported

• Types of substance(s) used
  ○ Benzodiazepine
• Eligibility for repeat treatments
  ○ Clinician referral or approval
• Program elements used in repeat treatments
  ○ Medication
• Where are repeat treatments provided
  ○ Outpatient
• Outpatient
  ○ Health outcomes
	There is very limited evidence to support an approach to facilitate benzodiazepine discontinuation among chronic benzodiazepine users (34)	High	No	11/11	2017	No	Not reported

• Types of substance(s) used
  ○ Opioids
• Program elements used in repeat treatments
  ○ Medication (e.g., opioid or other substance replacement therapy)
• Outcomes
	Deep brain stimulation (DBS) as a treatment for opioid use disorder (OUD) reduces craving and consumption of opioids in both human and animal subjects (30)
	• Substance-use disorder is defined as "a neuropsychiatric disorder identified by
		High	No	5/9	2021	Not available	None

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
• Health outcomes	a relapsing desire to take the drug despite negative consequences" • Clinical studies included in the review had patient populations who had failed to quit opioids after previous treatments • Reviews studies that examine the impacts of DBS on OUD ○ DBS is a "neurosurgical procedure that enables circuit-based targeted neuromodulation of deeper brain regions" • Clinical studies found that DBS increased patients' ability to remain abstinent; had positive impacts on their mental health, mental capacities and quality of life • Adverse impacts of DBS include confusion, urinary incontinence, fever, headache, epileptic seizures (in a patient who previously suffered epileptic seizures) and more discussed in the article						

• Types of substance(s) used
  ○ Alcohol
• Program elements used in repeat treatments
  ○ Psychotherapy
  ▪ Motivational interviewing
	Integrating self-affirmation interventions into motivational interviewing (MI) as a treatment for alcohol abuse by reducing defensiveness/resistance to treatment (35)
	• MI is a therapeutic tool designed to encourage behavioural change in individuals who are resistant to such a change, and was designed to treat alcohol and drug abuse
	  ○ When applying MI, clinicians are meant to avoid directly confronting patient resistance
	• Self-affirmation aims to affirm an image of self-integrity can decrease defensiveness, as well as increasing behavioural intentions and promoting health behavioural change
	• Studies have shown that self-affirmation may be more effective in
		Low	No	1/9	Not available	None	None

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
	conjunction with MI for those at greater risk levels due to alcohol abuse • No definition of substance-use disorder was provided						

• Types of substance(s) used
  ○ Opioids
• Program elements used in repeat treatments
  ○ Other
	Non-invasive brain stimulation (NIBS) has shown some promise as a treatment for OUD, with preliminary positive results for withdrawal/detoxification, opioid cravings, and reducing exposure to opioids and risk of developing OUD (31)
	• OUD is defined as "a chronic brain disease with negative consequences that include loss of control and lasting disruptions in neurocircuitry"
	• Particular NIBS techniques examined in this review include repetitive transcranial magnetic stimulation (rTMS), transcranial direct current stimulation (tDCS), and auricular vagus nerve stimulation (aVNS)
	• aVNS showed promise for treating symptoms of withdrawal
	• No literature was found regarding NIBS and maintenance treatment/prevention of relapse for OUD, although there are preliminary positive results for the use of NIBS in treating other substance-use disorders
	• rTMS and tDCS showed initial positive effects of reducing cravings in individuals with chronic OUD
		High	No	3/9	2019	None	None

• Types of substance(s) used
  ○ Opioids
  ▪ Prescription opioids
  ▪ Heroin
• Program elements
  ○ Additional supports following treatment
• Where is treatment provided
  ○ Inpatient/residential treatment
	Shared decision-making and providing treatment options for people with opioid use disorder may be beneficial (8)
	• The review identified the impact of shared decision-making in the treatment of opioid use disorder, where most treatment options were patient-regulated methadone dosing compared to fixed dosing, optional or mandatory counselling, home or office
		High	No	6/9	September 2019	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
○ Outpatient (e.g., with support from community-based organization or other community groups)	buprenorphine inductions, and inpatient or outpatient treatment • Shared decision-making may promote improvements on substance use, retention to treatment, quality of life, arrest rates and satisfaction with care						
• Types of substance(s) used ○ Opioids ○ Alcohol • Program elements ○ Additional supports following treatment • Where is treatment provided ○ Mixed inpatient and outpatient model (e.g., with a stepped approach down to lower levels of care intensity) • Outcomes ○ Patient experience	There are varying pre- and post-discharge strategies in addition to reported barriers and facilitators, which made it challenging for the authors to conclude on the impact of strategies to support substance-use disorder care transitions from acute-care to community-based settings (24) • Outcome measures were any visit following discharge, length of time retained in treatment post-discharge and time to first visit post-discharge • Pre-discharge strategies included discussing treatment options, scheduling appointments, providing contact list of treatment providers, sending electronic referrals, and linking patients to community treatment providers prior to discharge • Post-discharge strategies include bridge prescription (e.g., buprenorphine or outpatient prescription), transportation assistance, follow-up calls or texts, peer support and care navigation • Reported barriers included limited staff capacity, slow uptake of novel protocols, bias and stigma of the patient population and undertreatment of withdrawal • Reported facilitators included leveraging existing partnerships with community-based providers, building trust and continuity across settings and keeping open lines of communication	High	No	4/9	2021	No	None identified
• Types of substance(s) used ○ Alcohol	There is high quality evidence to suggest that Alcoholics Anonymous and Twelve-Step Facilitation are more effective than	High	No	10/11	2019	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations

• Care models
  ○ 12-step approach
• Where is treatment provided
  ○ Outpatient (e.g., with support from community-based organization or other community groups)
• Outcomes
  ○ Health outcomes
  ○ Cost
	other clinical interventions for abstinence and led to substantial healthcare cost savings among people with alcohol use disorder (1)
	• The Cochrane review compared Alcoholics Anonymous/Twelve-Step Facilitation compared to other clinical interventions (e.g., CBT) among people aged 18 years and older with alcohol use disorder or dependence						

• Types of substance(s) used
  ○ Alcohol
• Program elements
  ○ Medication (e.g., opioid or other substance replacement therapy)
• Outcomes
  ○ Health outcomes
• Priority populations
  ○ People who are homeless or marginally housed
	A recently updated systematic review on pharmacotherapy for adults with alcohol use disorder reported that acamprosate, topiramate and oral naltrexone had moderate strength of evidence for preventing return to any drinking among people with alcohol use disorder (11)
	• The use of oral naltrexone (50 mg) and acamprosate and topiramate have moderate strength of evidence on their impact on alcohol use disorder
	• There is low strength of evidence about injectable naltrexone in the reduction of drinking days and heavy drinking days among people experiencing homelessness
	• There was low strength of evidence for baclofen and disulfiram
		High	No	7/11	2022	No	None identified

• Types of substance(s) used
  ○ Alcohol
• Program elements
  ○ Medication (e.g., opioid or other substance replacement therapy)
• Outcomes
  ○ Health outcomes
	There was insufficient evidence to support the use of gabapentin for inpatients with acute alcohol withdrawal syndrome (13)	High	No	8/11	2022	No	None identified

• Types of substance(s) used
  ○ Alcohol
• Where is treatment provided
  ○ Inpatient/residential treatment
• Program elements
	While one study found that naltrexone initiation reduced 30-day hospital admissions, there is not enough available evidence to determine the impact of naltrexone initiation in the emergency department or inpatient setting for the management of alcohol use disorder (12)	High	No	4/9	31 October 2019	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
○ Medication (e.g., opioid or other substance replacement therapy) • Outcomes ○ Health outcomes							
• Types of substance(s) used ○ Alcohol • Concurrent mental health conditions • Care models ○ 12-step approach • Program elements ○ Psychotherapy ○ Medication (e.g., opioid or other substance replacement therapy) • Where is treatment provided ○ Inpatient/residential treatment • Outpatient (e.g., with support from community-based organization or other community groups)	Despite the availability of evidence-based pharmacotherapeutics approved for the treatment of alcohol use disorder, patients often experience barriers to the use of these medications, highlighting the need for efforts to increase the rates of prescribing among providers (14) • Hospital-based facilities were found to have higher odds of offering psychiatric medications and mental health services compared to outpatient and residential facilities for older adults with alcohol use disorder • Perceived barriers to obtaining pharmacotherapy for the treatment of alcohol use disorder in outpatient or residential settings included lack of knowledge, concerns about efficacy, complexity of prescribing, treatment philosophy and stigma, and medication accessibility including formulary restrictions as well as geographical and socioeconomic barriers	High	No	4/9	2020	No	Personal characteristics associated with discrimination (e.g. age, disability)
• Types of substance(s) used ○ Alcohol • Program elements ○ Medication (e.g., opioid or other substance replacement therapy) • Where is treatment provided ○ Inpatient/residential treatment • Priority populations ○ Veterans ○ People with a comorbid mental health issue ○ Black people, and other people of colour (i.e., Asian, Pacific Islanders, Latinx)	Medications for alcohol use disorder (MAUD) were only prescribed to 7% of patients admitted to the hospital experiencing alcohol withdrawal symptoms (AWS), with limited knowledge, patient vulnerability, organizational prioritization and patient characteristics cited as barriers to the initiation of MAUD (36) • Patients under 65, non-African Americans, Latinos and women were more likely to be prescribed MAUD for AWS	Medium	No	1/9	Published 2022	No	Personal characteristics associated with discrimination (e.g. age, disability)

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
• Outcomes • Patient experience							

• Types of substance(s) used
  ○ Alcohol
• Concurrent mental health conditions
  ○ Bipolar disorder
  ○ Depressive disorders
• Program elements
  ○ Psychotherapy
  ○ Medication (e.g., opioid or other substance replacement therapy)
  ○ Additional supports following treatment
• Where is treatment provided
  ○ Outpatient (e.g., with support from community-based organization or other community groups)
• Priority populations
  ○ People with a comorbid mental health issue
• Outcomes
• Health outcomes
	Adding XR-naltrexone to common psychosocial interventions treating alcohol use disorder generally resulted in significant improvements in heavy drinking, but not for patients with concurrent mental health conditions who were actively drinking (26)
	• Four studies of oral naltrexone that allowed active drinking at enrolment found no significant effect on heavy drinking, and all enrolled patients had comorbid major depression, bipolar disorder or cocaine use disorder
		High	No	7/11	2019	No	None identified

• Types of substance(s) used
  ○ Alcohol
• Concurrent mental health conditions
  ○ Anxiety disorders
  ○ Bipolar disorder
  ○ Borderline personality disorder
  ○ Depressive disorders
  ○ Eating disorders
  ○ Post-traumatic stress disorder
• Care models
  ○ 12-step approach
  ○ Stepped care model
  ○ Continuing care model
• Program elements
  ○ Psychotherapy
  ▪ Cognitive behavioural therapy
  ▪ Motivational interviewing
  ▪ Therapeutic communities
	Compared to medical/medication interventions, psychological/psychosocial and technological interventions were more likely to demonstrate improved treatment engagement and recovery (5)
	• Interventions included medical/medication, psychological/psychosocial, technological (e.g., smartphone app for self-management), mutual-help and combined approaches
	• Medications may offer a high level of feasibility but low level of acceptability due to documented side effects
	• Combining elements of case management, motivational enhancement and relapse prevention, medication management and treatment
		High	No	5/11	2019	No	None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
○ Medication (e.g., opioid or other substance replacement therapy) ○ Additional supports following treatment • Where is treatment provided ○ Inpatient/residential treatment ○ Outpatient (e.g., with support from community-based organization or other community groups) ○ Mixed inpatient and outpatient model (e.g., with a stepped approach down to lower levels of care intensity) • Priority populations ○ Veterans ○ People who have been previously admitted to inpatient treatment programs ○ People with a comorbid mental health issue ○ People with other medical conditions ○ People who are homeless or marginally housed • Outcomes • Health outcomes	referrals might improve follow-up treatment and long-term recovery rates						
• Types of substance used ○ Opioids ▪ Prescription opioids ▪ Heroin ○ Alcohol • Concurrent mental health conditions • Program elements ○ Psychotherapy ▪ Cognitive behavioural therapy ▪ Motivational interviewing ▪ Therapeutic communities • Length of time of treatment program • Where treatment is provided ○ Inpatient/residential • Priority populations	Results largely demonstrate that residential treatment is associated with significant social improvements, but limitations about the effectiveness of specific components are limited due to heterogeneity in the included studies (21) • Significant variance in treatment components were found across the studies with treatment lengths varying from 28 days to 12 months • Core components of included residential treatment include withdrawal and medication management, psychological treatment including both individual and group (motivational interviewing, CBT and mindfulness-based techniques) as well	High	No	5/10	2018	No	None reported

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
○ People with comorbid mental health issue • Outcomes ○ Health outcomes	as auxiliary services such as spiritual guidance and a range of social, employment and sexual health supports • Results largely demonstrate that residential treatment is associated with significant social improvements, with most studies being of moderate to strong quality • Positive effects were found for integrated treatment models for comorbid mental illness and substance dependence on substance use, mental health, social functioning and perceived quality of life • Definitive findings from the study are limited due to the heterogeneity among treatment approaches						
• Types of substance(s) used ○ Opioids ○ Alcohol • Where is treatment provided ○ Inpatient/residential treatment • Outcomes ○ Health outcomes	Evidence generally shows improvements among individuals with substance-use disorders participating in residential treatment, and management alcohol programs in hospital settings are effective and safe (22) • Moderate to weak evidence suggests that patients with substance-use disorders are more likely than those receiving no service to complete treatment and be considered abstinent, but results from comparisons to outpatient treatment remain uncertain • Strong to weak quality evidence found that residential treatment was effective for patients with substance use at improving substance use outcomes, social outcomes, reducing criminal activity and improving mental health outcomes • The evidence synthesis found residential treatment to be associated with the poorest survival outcomes when compared to counselling and	High	No	6/10	2018	Yes	Not reported

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
	other treatments in the first-year post-treatment • There is evidence that managed alcohol programs in the community improved drinking patterns, alcohol-related harms, criminal activity, mental health, and social and physical well-being						

• Types of substance(s) used
  ○ Opioids
  ○ Alcohol
• Concurrent mental health conditions
• Program elements
  ○ Psychotherapy
  ○ Additional supports following treatment
• Priority populations
  ○ People who have been previously admitted to inpatient treatment programs
  ○ People with a comorbid mental health issue
  ○ Indigenous peoples
  ○ Black people, and other people of colour
  ○ 2SLGBTQI+
• Where is treatment provided
  ○ Inpatient/residential treatment
• Outcomes
  ○ Health outcomes
	Clients entering residential treatment had comparably better outcomes when they had previous involvement in the justice system, had a high severity of substance use and had positive pre-treatment relationships with friends and family (25)
	• The review found a number of contexts influenced the effectiveness of treatment for substance-use disorder, including substance related problem severity, psychiatric comorbidities, diverse populations, pre-treatment relationships, lack of structure and a lack of coping strategies
	• Each of criminal justice involvement, previous treatment and high substance use severity led to better outcomes for residential users, largely as a result of higher motivation to engage with treatment
	• Mixed effects were identified for the effects of psychiatric comorbidities, with most finding that they led to improved outcomes among residential clients, but others found they increased the likelihood of readmission
	• The review notes that this is a result of a lack of behavioural resources to support coping skills
	• Diverse populations were found to have positive experiences when spiritual and traditional elements were
		High	No	4/9	2020	No	Race/ethnicity/ culture/ language
							
							Time-dependent relationships

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
	present, as well as space to discuss sexuality and gender concerns • Individuals with positive pre-treatment relationships had better outcomes than those with strained or dysfunctional relationships						

• Types of substance(s) used
• Program elements
  ○ Psychotherapy
  ○ Medication
  ○ Additional supports following treatment
• Where treatment is provided
  ○ Inpatient/residential treatment
  ○ Outpatient
• Priority populations
  ○ Indigenous peoples
• Outcomes
  ○ Health outcomes
  ○ Patient experience
	Both residential and non-residential treatment programs resulted in improved rates of abstinence at 12 and 24 months; it remains uncertain which approach is most beneficial, but the synthesis noted that the provision of culturally appropriate care was critical to ensuring positive results (23)
	• This evidence synthesis examines the effects of residential and non-residential treatment programs attended by Indigenous individuals
	• Most included studies examined the effects of residential treatment, though a few examined both residential and non-residential treatment
	• Common treatment models in residential programs include detoxification, 12-step abstinence, dialectical behaviour therapy, land-based cultural camps and culture as treatment
	• For residential treatment, rates of abstinence ranged from 30% to 96% 12 months post-treatment
	• Non-residential treatment included community-based programming, 12-step programs, talking circles, pharmacotherapy or substitution therapy, behavioural support groups and group therapy
	• Rates of reported abstinence for non-residential treatment participants ranged from 46% to 90% at 24 months post-treatment
		High	No	5/9	2017	No	Race/ethnicity/ culture/ language

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
	• Mixed results were found for comparisons of residential and non-residential treatments • Many programs included cultural components that were critical to treating Indigenous populations; these included practices such as sweat lodge ceremonies, smudging, drumming and healing circles as well as traditional activities of fishing and hunting						

• Types of substance(s) used
  ○ Alcohol
• Concurrent mental health conditions
  ○ Borderline personality disorder
• Program elements
  ○ Psychotherapy
  ▪ Dialectic behavioural therapy
  ○ Where is treatment provided
  ▪ Outpatient
• Priority populations
  ○ People with comorbid mental health issues
• Outcomes
  ○ Health outcomes
	Integrated CBT holds promise as a treatment for adolescents, while dialectic behaviour therapy may be helpful for alcohol patients with borderline personality disorder, but these findings are based on a relatively small sample of patients (2)
	• This synthesis aims to examine the effects of interventions designed to prevent suicide and reduce self-harm as well as alcohol consumption on those with alcohol problems
	• Problematic alcohol use was defined either by meeting criteria for an alcohol use disorder, alcohol dependence or abuse, or alcohol consumption of five or more standard drinks for men and four for women per occasion within the last 30 days
	• All interventions focused on outpatient settings, except for one for which online services were provided
		High	No	3/9	2020	No	

Appendix 4: Detailed data extractions from single studies about models of care for repeat treatment for substance use

Dimension of the organizing framework	Relevance rating	Study characteristics	Sample and intervention description	Declarative title and key findings

• Types of substance(s) used
  ○ Opioids
• Eligibility for repeat treatments
• Time since last substance use
• Program elements used in repeat treatment
  ○ Psychotherapy
  ○ Contingency management
  ○ Medication
• Where are repeat treatment provided
  ○ Outpatient
• Financing for repeat treatment models
  ○ Public payment
• Outcomes
  ○ Health outcomes
  ○ Cost
	High	*Focus of study:* Examining the efficacy and cost-effectiveness of personalized psychosocial intervention alongside opioid agonist therapy for those with chronic treatment-resistant opioid use
		
		Publication date: 2019
		
		Jurisdiction studied: United Kingdom
		
		Methods used: Randomized controlled trial
			136 patients were eligible if they met the criteria or opioid or cocaine dependence, or in the past 12 months had voluntarily sought continued oral maintenance opioid agonist therapy, which they had been prescribed for at least six week. All participants were treatment resistant, which meant that had used illicit or non-prescribed opioids or cocaine on one or more days in the past 28 days. Those receiving the experimental condition received a personalized psychosocial intervention, made up of psychological change methods including contingency management and recovery activities, in addition to treatment as usual.	An adjunctive personalized psychosocial intervention in addition to standard agonist therapy was efficacious and cost-effective compared with standard therapy alone in helping treatment-resistant patients (6)
				• The psychosocial intervention had a higher probability of being cost-effective than treatment as usual
				• Quality adjusted life years were higher in the psychosocial intervention group than the control group with a 60–67% probability of being cost effective at the U.K. willingness to pay threshold of £20,000 to 30,000 per quality-adjusted life year

• Types of substance(s) used
  ○ Opioids
• Eligibility for repeat treatments
• Time since last substance use
• Program elements used in repeat treatment
  ○ Psychotherapy
  ○ Medication
• Where are repeat treatment provided
  ○ Outpatient
• Outcomes
  ○ Health outcomes
  ○ Costs
	High	*Focus of study:* Comparing the effectiveness and cost effectiveness of diacetylmorphine compared to methadone maintenance therapy for those with chronic opioid dependence
		
		Publication date: 2012
		
		Jurisdiction studied: Canada
		
		Methods used: Modelling
			Compared supervised, medically prescribed diacetylmorphine and optimized methadone maintenance treatment in people with chronic opioid dependence and multiple failed treatment attempts. Both the experimental and control treatment approaches included a comprehensive range of psychosocial services and primary care services.	Diacetylmorphine may be more effective and less costly than methadone among people with chronic opioid dependence refractory to treatment (19)
				• Diacetylmorphine is more effective than methadone maintenance treatment in retaining opioid-dependent patients in treatment and improving health and social functioning, specifically for people with opioid dependence refractory to treatment who are at high risk of adverse health consequences and engagement in criminal activities
				• For cost effectiveness, those receiving diacetylmorphine gained 7.92 discounted quality-adjusted life years (compared to 7.46 using standard methadone maintenance therapy) and generated a lower societal cost

• Types of substance(s) used
  ○ Opioids
  ○ Heroin
	High	*Focus of study:* Comparing supervised injection heroin, supervised injection methadone	Treatment resistant chronic opiate-dependent patients receiving oral substitution treatment for at least	Supervised injectable heroin treatment and supervised injectable methadone treatment showed no clearly identified benefit over optimized oral methadone in

Dimension of the organizing framework	Relevance rating	Study characteristics	Sample and intervention description	Declarative title and key findings

• Eligibility for repeat treatment
• Where are repeat treatments provided
  ○ Outpatient
• Outcomes
  ○ Health outcomes
		and oral methadone treatment for chronic opioid use
		
		Publication date: 2014
		
		Jurisdiction studied: United Kingdom
		
		Methods used: Randomized control trial
			six months preceding recruitment who were still injecting street heroin on most days. Patients were randomly assigned to receive supervised injectable heroin or supervised injectable methadone and had the option of having a supplementary dose of prescribed oral methadone.	terms of wider drug use, crime or physical or mental health over a six month period, though they did reduce street heroin use (16)
				• At six months, no significant differences were found between treatment groups in wider drug use or physical or mental health

• Types of substance(s) used
  ○ Alcohol
• Program elements used in repeat treatments
  ○ Additional supports (case manager)
• Where are repeat treatments provided
• Outpatient
  ○ Outcomes
  ○ Costs
	High	*Focus of study:* Cost effectiveness of a navigator-based intervention for individuals experiencing repeat admissions for detoxing
		
		Publication date: 2019
		
		Jurisdiction studied: United States
		
		Methods used: Cost-effectiveness analysis
			Patients in a Massachusetts Medicaid population with multiple admissions to detox centres used recovery support navigators who were trained to effectively engage and connect clients with substance-use disorder follow-up care and community resources.	Though the results of the study were not significant, they demonstrate potential for insurers to reduce the healthcare costs of repeat detoxification centre visits by using a navigator-based intervention (27)
				• Costs were reduced by USD $68 per month for intervention-enrolled members than for others and the intervention was associated with shifts in the healthcare service mix from more to less acute settings

• Types of substance(s) used
• Concurrent mental health conditions
  ○ Bipolar disorder
  ○ Borderline personality disorder
• Eligibility for repeat treatments
  ○ Referral or approval from another authority
• Care model used in repeat treatments
  ○ Continuing care
• Program elements used in repeat treatments
  ○ Psychotherapy
  ○ Medication
• Where are repeat treatments provided
  ○ Inpatient
• Priority populations
  ○ People who are homeless or marginally housed
	High	*Focus of study:* Treatment at a compulsory treatment facility for homeless individuals with dual-diagnosis
		
		Publication date: 2019
		
		Jurisdiction studied: Netherlands
		
		Methods used: Observational study
			Compulsory treatment facility for long-term care for homeless individuals with dual-diagnosis who are seen as treatment-resistant by the existing services (and may include previous compulsory admissions). Individuals are referred on the basis of involuntary admission by the municipal health services of three major Dutch cities and are admitted on the basis of a court order.	Long-term involuntary treatment drawing on a wide-range of disciplines can be helpful for some subsets of treatment-resistant dual-diagnosis individuals (32)
				• Three groups of patients, the first was the discharged group that consisted of patients for whom treatment had been successful, the second is the continued care group that consisted of patients who were still hospitalized after a minimum of four years and the third is the referred group who had transferred to a more restrictive setting
				• Treatment is delivered by multidisciplinary teams and is provided within a healing community made up of individual houses
				• The study found that marked improvements were possible among a substantial number of patients, many of whom were discharged within four years and demonstrated improvements in psychiatric symptoms, self-care behaviour, verbal skills and disability

Dimension of the organizing framework	Relevance rating	Study characteristics	Sample and intervention description	Declarative title and key findings
• Outcomes ○ Health outcomes				• Health outcomes improved among those who remained in the in-treatment facility • Among those for whom the treatment did not work, these individuals often displayed substantially more behavioural problems and oppositional behaviour than others

• Types of substance(s) used
  ○ Opioids
  ○ Benzodiazepine
• Eligibility for repeat treatment
  ○ Clinician referral or approval
• Program elements used in repeat treatment
  ○ Psychotherapy
  ○ Medication
  ○ Other
• Where are repeat treatments provided
  ○ Outpatient
• Outcomes
  ○ Health outcomes
	High	*Focus of study:* Examine the effectiveness of deep brain stimulation for severe treatment refractory opioid and benzodiazepine use
		
		Publication date: 2022
		
		Jurisdiction studied: United States
		
		Methods used: Observational
			A single individual in their early 30s with a 10-year history of severe treatment refractory opioid and benzodiazepine use disorders received deep brain stimulation of the nucleus accumbens/ventral capsule.	In a single individual, deep brain stimulation was found to be safe and resulted in abstinence from illicit substance use throughout 12 months of follow-up (29)
				• The individual continued to be actively engaged and compliant with comprehensive treatment including medications for opioid use disorder using buprenorphine/naloxone, individual and group therapy and participation in support groups

• Types of substance(s) used
  ○ Opioids
• Program elements used in repeat treatments
  ○ Medication (e.g., opioid or other substance replacement therapy)
• Where are repeat treatments provided
  ○ Outpatient (e.g., with support from community-based organization or other community groups)
• Priority populations for repeat treatments
  ○ Veterans
	High	*Focus of study:* Effectiveness of Buprenorphine Extended-Release (BUP-XR) for treating chronic opioid use disorder (OUD)
		
		Publication date: May 2022
		
		Jurisdiction studied: United States
		
		Methods used: Retrospective data collection from medical records
			Twenty-six treatment-resistant veterans across two Veterans Affairs outpatient substance-use disorder (SUD) clinics who were described as clinically and medically complex. BUP-XR is a subcutaneous injection delivered to participants.	BUP-XR as a treatment for OUD in veterans showed strong retention in addition to reduction in emergency department visits, length of hospitalization, opioid misuse and homelessness (17)
				• BUP-XR is an extended-release medication that is an alternative treatment for patients who have difficulty adhering to daily medication
				• Treatment retention was strong, with 81% receiving six or more injections
				• 70% had one late dose of BUP-XR, and 19% had a break in treatment
				• 57.7% were negative for non-prescribed opioids throughout treatment
				• Emergency department visits, length of hospital stay, and homelessness decreased
				• No definition of substance-use disorder was provided

• Types of substance(s) used ○ Opioids • Care models used in repeat treatments	High	*Focus of study:* To explore what factors may contribute to the likelihood an individual will undergo five or more treatments	249,769 (52,095 opioid and 197,674 heroin) records of individuals who have received care from a substance abuse treatment	Evidence from the datasets revealed that there are factors that have an association with treatment resistance (37)

Dimension of the organizing framework	Relevance rating	Study characteristics	Sample and intervention description	Declarative title and key findings
○ 12-step approach • Program elements used in repeat treatments ○ Psychotherapy ○ Cognitive behavioural therapy ○ Motivational interviewing ○ Medication (e.g., opioid or other substance replacement therapy) • Where are repeat treatments provided ○ Inpatient/residential treatment • Outcomes ○ Health outcomes ○ Patient experience		*Publication date:* 2021 *Jurisdiction studied:* United States *Methods used:* Secondary data analysis	facility were identified from the Treatment Episode Data Set (TEDS-A-2017). Secondary analysis of a dataset of patients' admissions into SUD treatment to identify ranges or sets of profiles that might foretell treatment resistant opioid use disorder (TROUD).	• Patients that used injection as their route of administration had nearly three times the likelihood of repeating treatment attempts five or more times in comparison with those who used another method of administration • Patients that come to a treatment facility with an opioid or heroin disorder and meet all the high-risk categories have more than a 50% chance of treatment resistance; those who meet the low-risk category criteria are unlikely to experience treatment resistance • High risk categories include high education, not employed, homeless/dependent living arrangement, injection as route of administration, use daily, started using at age 20 or under, co-occurring mental and substance-use disorders, age 30–64 years at admission, male, never married, and other race category
• Types of substance(s) used ○ Opioids ○ Heroin • Concurrent mental health conditions ○ Bipolar disorder ○ Eligibility for repeat treatments ○ Clinician referral or approval • Care models used in repeat treatments ○ Continuing care model ○ After-care model • Program elements used in repeat treatments ○ Psychotherapy ○ Cognitive behavioural therapy ○ Therapeutic communities ○ Medication (e.g., opioid or other substance replacement therapy) ○ Additional supports following treatment • Where are repeat treatments provided ○ Mixed inpatient and outpatient model (e.g., with a stepped	High	*Focus of study*: To compare the long-term outcomes of treatment-resistant bipolar 1 heroin addicts with peers without comorbidity *Publication date:* 2013 *Jurisdiction studied:* Italy *Methods used:* Prospective cohort study, observational	104 heroin-dependent patients who also met criteria for treatment resistance. 41 met DSM-IV-R criteria for Bipolar 1 Disorder (BIP1-TRHD) and 63 were without psychiatric comorbidity (NDD-TRHD). Members of the group were followed in a naturalistic approach for a minimum of 0.5 and a maximum of 8 years in the context of a methadone programme, using retention in treatment and rates of heroin use as end parameters.	Treatment-resistant patients with bipolar 1 disorder psychiatric comorbidity showed a better long-term outcome than those without psychiatric comorbidity in a high-threshold, high dose methadone program (20) • Differences in educational level, duration of heroin addiction, level of heroin use, and age at first addiction treatment did not appear to be related to better retention or outcome in the BIP1-TRHD patients • BIP1-TRHD patients, and especially women, were retained in treatment for longer and required higher doses of methadone than NDD-TRHD patients • For non-compliant patients with a bipolar 1 diagnosis, a flexible dosing regimen that permits the administration of higher doses may lead to higher retention rates • The long-term maintenance of medication may be important factors in satisfactory outcomes in bipolar 1 patients treated with higher dosages

Dimension of the organizing framework	Relevance rating	Study characteristics	Sample and intervention description	Declarative title and key findings
approach down to lower levels of care intensity) • Outcomes o Health outcomes o Patient experience				
• Types of substance(s) used o Alcohol o Program elements used in repeat treatments o Psychotherapy o Multimodal behavioural therapy o Additional supports following treatment • Length of time of repeat treatment programs • Where are repeat treatments provided o Outpatient (e.g., with support from community-based organization or other community groups) • Outcomes o Health outcomes o Patient experience	High	*Focus of study:* To implement and evaluate unilateral family therapy (UFT) for alcohol abuse, assisting the non-alcoholic spouse in helping their alcohol-abusing partner enter treatment and/or reduce drinking *Publication date:* 2020 *Jurisdiction studied:* United States *Methods used:* Randomized controlled trial	42 nonalcohol-abusing spouses participated in this randomized control trial, and 13 no-treatment spouses served as an additional comparison group. UFT consists of three phases of treatment. The first phase prepares the nonalcohol-abusing spouse to assume a rehabilitative role and enhance their influence potential. Phase II involves arranging interventions intended to get the abuser into treatment, reduce the drinking or both. Phase III involves maintaining spouse and abuser treatment gains.	Unilateral family therapy was found to be successful in facilitating treatment entry, drink reduction and long-term improvement in psychological health and marital functioning (4) • Improvement was reported in drink-related characteristics, spouse psycho-logical variables, spouse role induction variables and family/relationship factors; there was also strong support suggesting that alcohol-related distress was reduced due to treatment • Repeated measures results show limited support for a reduction in abusers' drinking levels • There were four limitations to the UFT study: the study took place about 30 years ago, the limited diversity of the sample, the suboptimal randomization, and lower confidence of the statistical interpretation
• Types of substance(s) used o Alcohol o Opioids o Other • Where are repeat treatments provided o Outpatient (e.g., with support from community-based organization or other community groups) • Outcomes o Patient experience	Medium	*Focus of the study:* To assess the service pathway between adult acute mental health inpatient units and local alcohol tobacco and other drugs services *Publication date:* 2020 *Jurisdiction studied:* Australia *Methods used:* Cohort study	Inpatients admitted to adult acute mental health inpatient units, who had a SUD diagnosis in accordance with ICD-10 to determine whether they attended alcohol tobacco and other drug services in the local community within 30 days of their discharge.	Post-discharge attendance was very low despite the emphasis on substance-use treatment, and while comorbid substance use psychotic disorder was very common it was correlated with less frequent attendance following discharge (38) • The group with the highest attendance rate following discharge was that with a substance-use disorder only and the attendance of patients with a primary psychotic disorder was very low
• Types of substance(s) used o Opioids o Heroin o Eligibility for repeat treatment o Clinician referral or approval	Medium	*Focus of study:* Comparing prescription heroin treatment to standards methadone maintenance therapy among chronic heroin-dependent individuals	Patients enrolled in the trials were at least 25 years old and had regularly attended methadone maintenance programmes during the previous six months but continued to use illicit heroin	Treatment-resistant heroin dependence was better treated with a combined treatment of methadone and prescription heroin than heroin alone, but these findings are from two relatively small trials (39) • Some patients with chronic heroine dependence are offered new therapies after first-line

Dimension of the organizing framework	Relevance rating	Study characteristics	Sample and intervention description	Declarative title and key findings

• Program elements used in repeat treatment
  ○ Psychotherapy
  ○ Medication
• Where are repeat treatments provided
  ○ Outpatient
• Outcomes
  ○ Health outcomes
		Publication date: 2004
		
		Jurisdiction studied: Netherlands
		
		Methods used: Logistic regression
			nearly daily. Patients in the experimental groups were referred to a newly established heroin treatment unit and were offered prescription heroin for seven days per week and three times per day, with a maximum of 400 mg per visit and 1,000 mg per day. This treatment was compared to standard methadone maintenance therapy. Both treatment were offered comparable standard psychosocial interventions.	methadone maintenance treatment has not succeeded in stabilizing the patient
				• The cost of supervised heroine treatment is quite expensive, approximately 15,000 euros per patient per year, with the majority of these costs stemming from personnel
				• Treatment response was significant higher in the 12-month methadone and heroin condition compared to 12-month methadone alone
				• Heroin-addicted patients with a history of abstinence-oriented treatment compared had a much higher response rate to heroin treatment compared to methadone treatment, while patients without a history of abstinence-oriented treatment do equally well in heroin-assisted treatment and methadone maintenance treatment

• Types of substance(s) used
  ○ Opioids
  ○ Heroin
• Eligibility for repeat treatment
  ○ Clinician referral or approval
• Program elements used in repeat treatment
  ○ Psychotherapy
  ○ Medication
• Where are repeat treatments provided
  ○ Outpatient
• Outcomes
  ○ Health outcomes
	Medium	*Focus of study:* Examining effectiveness of long-term heroin-assisted treatment for treatment-resistant heroin-dependent patients
		
		Publication date: 2010
		
		Jurisdiction studied: Netherlands
		
		Methods used: Observational cohort study
			Heroin-assisted treatment for treatment-resistant heroin-dependent patients.	Results from two long-term observational cohort studies demonstrate that it may be an effective treatment for those resistant to standard methadone maintenance therapies (40)
				• The response rate was significantly better for those continuing heroin-assisted therapy four years on to those that discontinued treatment
				• Continued heroin-assisted therapy was associated with fewer health problems and fewer illicit drugs and excessive alcohol use

• Types of substance(s) used
  ○ Opioids
  ○ Stimulants
  ○ Cocaine
• Eligibility for repeat treatments
  ○ Clinician referral or approval
• Program elements used in repeat treatments
  ○ Psychotherapy
  ○ Medication (e.g., opioid or other substance replacement therapy)
	Medium	*Focus of study:* To test a voucher-based abstinence reinforcement procedure to reduce opiate and cocaine use in treatment-resistant opiate- and cocaine-abusing methadone patients
		
		Publication date: 2001
		
		Jurisdiction studied: United States
			Participants were drawn from the treatment/research clinic of the Behavioral Pharmacology Research Unit, Johns Hopkins University School of Medicine. In Phase 1, using a within-subject design, treatment-resistant patients were required to take a 60 mg methadone dose daily and exposed to low- and high-magnitude voucher-based abstinence reinforcement interventions. In	The study found that voucher reinforcement produced modest improvements in treatment outcome in the treatment-resistant population (41)
				• Even though voucher earnings during the initial exposure to the procedures were intermediary to the low and high conditions, the percentage of negative urine samples was lower than under both conditions, likely relating to differences in treatment duration
				• In both phases, the percentage of negative opiate-only and cocaine-only samples under each voucher

Dimension of the organizing framework	Relevance rating	Study characteristics	Sample and intervention description	Declarative title and key findings
○ Additional supports following treatment • Where are repeat treatments provided ○ Inpatient/residential treatment • Outcomes ○ Health outcomes ○ Patient experience		*Methods used:* Within-subject, crossover design	Phase 2, the methadone dose was increased to 120 mg per day and patients were exposed to the low and high voucher magnitudes as in Phase 1.	condition was slightly higher than the percentage for both drugs • The findings provide further evidence that highly treatment-resistant heroin and cocaine use is modifiable with sufficient voucher reinforcer magnitude and methadone dose
• Types of substance(s) used ○ Opioids ○ Heroin • Eligibility for repeat treatment • Where are repeat treatments provided ○ In patient • Outcomes ○ Health outcomes	Medium	*Focus of study:* Examining the effects of adding brief motivational enhancing intervention to supervision as usual for offenders entering substance-use treatment *Publication date:* 2020 *Jurisdiction studied:* Netherlands *Methods used:* Observational cohort	220 offenders with substance use problems were entered into trial of adding brief motivation enhancing intervention to supervision as usual.	No significant difference was found for adding a brief motivational enhancing intervention to supervision as usual for offenders entering substance-use treatment (42)
• Types of substance(s) used ○ Opioids • Eligibility for repeat treatments • Time since last substance use • Program elements used in repeat treatment ○ Psychotherapy ○ CBT ○ Medication • Where are repeat treatment provided ○ Outpatient • Outcomes ○ Health outcomes	Medium	*Focus of study:* Examining the efficacy of combined interoceptive exposure CBT and methadone maintenance therapy for chronic opioid use *Publication date:* 2002 *Jurisdiction studied:* United States *Methods used:* Randomized controlled trial	23 outpatients failing available and accepted strategies to control illicit drug use, namely combination methadone treatment, counselling and contingency management. Failing treatment was determined if their illicit drug use continued despite three months in a methadone treatment program utilizing weekly counselling. Those with uncontrolled medical illness, schizophrenia, psychosis or bipolar disorder were excluded. CBT for interoceptive cues was delivered in 12 weekly sessions and three booster sessions scheduled for two weeks, one month and two months following completion.	New approaches that combine interoceptive exposure CBT with ongoing methadone maintenance therapy may be effective among women with chronic opioid dependence, but the sample studied was very small (43) • The new CBT approach emphasizes interventions to help patients tolerate and respond with self-control techniques including through cognitive coping procedures, over-rehearsed behavioural responses or relaxation or diaphragmatic breathing • In particular, this is focused on emphasizing interoceptive exposure plus cognitive restructuring • The treatment composed of four parts: an informational component, exposure to interoceptive cures of drug craving with rehearsal of adaptive responses, cognitive restructuring and somatic coping skills • The experimental treatment was more effective than combined CBT and methadone treatment among women but not among men

Dimension of the organizing framework	Relevance rating	Study characteristics	Sample and intervention description	Declarative title and key findings
				• While there was a reduction in the ongoing use of illicit drugs, no change was observed in depressed mood from either treatment

• Types of substance(s) used
  ○ Alcohol
• Care models
  ○ Stepped-care model
  ○ After-care model
• Program elements
  ○ Additional supports following treatment
• Length of time of treatment program
• Where is treatment provided
  ○ Mixed inpatient and outpatient model (e.g., with a stepped approach down to lower levels of care intensity)
	Medium	*Focus of study:* To describe a model of split hospitalization for severe alcohol use disorder
		
		Publication date: 2023
		
		Jurisdiction studied: Belgium
		
		Methods used: Perspective article describing a framework for care
			A three-week split hospitalization model of care for severe alcohol use disorder consisting of weeks 1 and 3 inpatient and week 2 outpatient settings	A 3-week inpatient care model involving 'split hospitalization' whereby patients attend an interdisciplinary care unit consisting of hepato-gastroenterology and psychiatry during weeks 1 and 3 and return home week 2 was proposed to help address stigma and denial associated with alcohol use disorder (44)
				• Stigma and denial present key barriers to treatment for patients with alcohol use disorder, highlighting the importance of flexible models of care

Appendix 5: Detailed jurisdictional scan about models of care for repeat treatment approaches for substance use in each of the 'Five Eyes' countries

Five Eye country	Description of funded programs for military personnel and Veterans for repeat treatment for substance use

Australia	• A specific list of programs and models for repeat treatment was not identified
	• Open Arms provides free face-to-face mental health counselling, group programs and peer support for Veterans and families including for substance use
	  ○ Open Arms provides referral options (which could be to other Open Arms)
	• Treatment for mental health conditions funded under the Non-Liability Health Care may include:
	  ○ treatment from a mental health provider such as a general practitioner, psychiatrist, psychologist, mental health social worker or mental health occupational therapist
	  ○ mental health admissions to a public or private hospital
	  ○ mental health treatment delivered at a day procedure facility
	  ○ prescribed medication for mental health conditions
	  ○ relevant pathology and medical imaging services required to assess and diagnose mental health conditions
	  ○ department of Veterans Affairs recognized alcohol and drug treatment programs.
	• Access to these is dependent on having a white treatment care which is for current or former Australian Defence Force member or a Commonwealth or Allied veteran with a service-related injury or condition accepted by your country of service
	• Mental health treatments funded by the Department of Defence or Department of Veterans Affairs are expected to be evidence based

Canada	• As of 1 April 2022, Veterans applying for a disability benefit for certain mental health conditions will now receive immediate mental health coverage, including treatment for service-related mental health conditions such as anxiety and depressive disorders, or trauma-and-stressor-related disorders • Benefits are organized by programs of choice, substance-related treatment is primarily focused on the coverage of outpatient psychologist, psychiatrist and counselling services for which coverage varies by type and by province • Other coverage for substance-use treatment may be provided under typical provincial health insurance
New Zealand	• Specialist mental health and addiction services, when required, will be arranged by Defence Health and are generally accessed through the public health system, though private providers may be used • Through the public system there are both inpatient and outpatient programs that may be accessed • Live in services such as residential services and support houses may have costs associated with them, but many are free and run by non governmental organisations • Outpatient services covered by regional health systems include some individual and group counselling, withdrawal management, day programs, and medication-assisted treatment, no specific limits were identified
U.K.	• There are specific mental health and addictions programs in the U.K. that have been developed to support Veterans, namely Op Courage, which provides support and treatment for substance misuse and addictions as well as support for Veterans in accessing NHS supports • In addition, Veterans may access services provided by the NHS local drug service, charitable organizations or private drug and alcohol organizations • NHS local drug services include talk therapy such as CBT as well as medication assisted treatment, inpatient and outpatient detoxification, support groups and other harm reduction services • The NHS does not operate its own residential treatment facilities it is possible to consult with outside groups that provide the service for free • U.K. hospitals offer residential detoxification and short-term rehabilitation supports, and most local drug services offer drug service coordination to determine the right approach for care, including coordinating and seeking funding for inpatient drug treatment

Five Eye country	Description of funded programs for military personnel and Veterans for repeat treatment for substance use
U.S.	• In the U.S., Veterans Affairs (VA) provides a range of medication options including medically managed detoxification programs and drug substitution therapies as well as many counselling options such as short-term outpatient counselling, intensive outpatient treatment, residential live-in care, and relapse prevention • These programs can all be accessed through a VA primary care provider who will screen for substance use problems and concurrent conditions • For Veterans not eligible for VA healthcare benefits, private counselling, alcohol and drug assessment and other support is provided for those who served in a combat zone at no cost ○ In addition, separate programs are available for Veterans who are homeless • Factors such as income level, disability rating and military service history may alter whether a co-payment is required

Appendix 6: Documents excluded at the final stages of reviewing

Document type	Hyperlinked title
Evidence synthesis	Comparison of treatment options for refractory opioid use disorder in the United States and Canada: A narrative review
	Psychological interventions for co-occurring depression and substance use disorders
	Psychosocial interventions for benzodiazepine harmful use, abuse or dependence
Single study	Multiple previous detoxifications are associated with less responsive treatment and heavier drinking during an index outpatient detoxification
	Treatment-refractory substance use disorder: Focus on alcohol, opioids, and cocaine
	Reasons for entering treatment reported by initially treatment-resistant patients with substance use disorders
	High-dose of baclofen for treatment-resistance alcohol dependence
	Treatment of severe alcohol withdrawal

Waddell K, Jaspal A, Demaio P, Bhuiya A, Phelps A, Wilson MG. Rapid evidence profile 62: Examining the effects of care models and program elements of repeat treatment approaches for substance use and concurrent mental health conditions. Hamilton: McMaster Health Forum, 12 February 2024.

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