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

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Context

- Substance-use-related deaths continue to increase in Canada, as does the toxicity of the illegal drug supply and the rate of hospitalizations and emergency department visits.(1)
- Many of the treatment approaches that have been used to support and treat individuals who use substances are not equally effective for all, with some individuals experiencing treatment resistance or treatment refractory.
- While a lot of research has been conducted on treatment-resistant mental health conditions, such as depression and bipolar disorder, relatively less examines treatment-resistant substance use and its co-occurrence with mental health conditions.

Questions

- What is known about care models (e.g., stepped, continuing and after-care models) and program elements (for each of inpatient, outpatient and aftercare) for repeat treatment of substance use with and without concurrent mental health conditions (including but not limited to PTSD)?
- What care models, program elements and repeat treatment for substance use with and without concurrent mental health conditions are publicly funded for Veterans in each of the 'Five Eyes' countries?

Box 1: Evidence and other types of information

+ Global evidence drawn upon

Evidence syntheses selected based on relevance, quality and recency of search

+ Forms of domestic evidence used (= Canadian)

Evaluation

Technology assessments

+ Other types of information used

Jurisdictional scan (five countries – Australia, Canada, New Zealand, United Kingdom, United States)

*** Additional notable features**

Prepared in five-business days using an 'all hands on deck' approach

High-level summary of key findings

- We identified 43 evidence documents relevant to the question, of which we deemed 34 to be highly relevant, including 24 evidence syntheses and 10 single studies.
- Included evidence documents rarely used the term repeat treatment and instead referred to individuals as being treatment resistant or treatment refractory, which requires an individual to have received previous substance-use treatment including psychotherapy and medication-assisted therapies for between six and 12 months and to have

continued using substances (beyond those prescribed as part of medication-assisted therapies) throughout and following treatment.

- The included evidence primarily addressed the use of opioids and alcohol and, despite relatively high rates of comorbidity, relatively few addressed co-occurring mental health conditions.
- Evidence documents found positive health outcomes from residential treatments that include withdrawal and medical management, psychological treatment, as well as auxiliary services including spiritual guidance, employment and sexual health services.
- Evidence documents identified improvements in health outcomes from motivational interviewing and unilateral family therapy, and mixed health outcomes for ketamine-assisted psychotherapy for individuals with treatment-resistant alcohol use.
- Evidence documents identified positive health outcomes from a stepped care model and extended-release buprenorphine, largely positive health outcomes from deep brain and non-invasive brain stimulation based on a small sample, while mixed health outcomes but higher retention rates were identified from supervised diacetylmorphine compared to methadone-maintenance therapy for individuals with treatment-resistant opioid use.
- Additional studies are needed to examine the effects of treatment models on co-occurring mental health conditions.

Framework to organize what we looked for

- Types of substance(s) used
  - Opioids
    - Prescription opioids
    - Heroin
    - Fentanyl
  - Stimulants

Box 2: Approach and supporting materials

We identified evidence addressing the question by searching Health Systems Evidence, Cochrane Database of Systematic Reviews, PubMed and PsychInfo. All searches were conducted on 14 December 2023. An additional set of searches focused on residential treatment and alcohol use disorder were completed on 12 January 2024 following feedback from the requestor. The search strategies used are included in Appendix 1. In contrast to synthesis methods that provide an in-depth understanding of the evidence, this profile focuses on providing an overview and key insights from relevant documents.

We searched for full evidence syntheses (or synthesis-derived products such as overviews of evidence syntheses), protocols for evidence syntheses and single studies. We identified jurisdictional experiences by hand searching government and stakeholder websites for information relevant to the question from each of the 'Five Eyes' countries (Australia, Canada, New Zealand, U.K. and the U.S.). The search strategies used, including which websites were searched for the jurisdictional scan, are included in Appendix 1.

We appraised the methodological quality of evidence syntheses that were deemed to be highly relevant using AMSTAR. AMSTAR rates overall quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality. The AMSTAR tool was developed to assess reviews focused on clinical interventions, so not all criteria apply to evidence syntheses pertaining to delivery, financial or governance arrangements within health systems or to broader social systems.

A separate appendix document includes:

1) methodological details (Appendix 1)
2) summary of key findings from highly relevant evidence documents (Appendix 2)
3) details about each identified evidence synthesis (Appendix 3)
4) details about each identified single study (Appendix 4)
5) details from jurisdictional scan of 'Five Eyes' countries (Appendix 5)
6) documents that were excluded in the final stages of review (Appendix 6).

        - Cocaine
        - Crack
        - Methamphetamine
    - Alcohol
    - Cannabis
    - Injected substances (unspecified type)
    - Other
- Concurrent mental health conditions
    - Anxiety disorders
    - Bipolar disorder
    - Borderline personality disorder
    - Depressive disorders
    - Eating disorders
    - Post-traumatic stress disorder
    - Schizophrenia
    - Others
- Care models
    - 12-step approach
    - Stepped care model
    - Continuing care model
    - After-care model
- Program elements
    - Psychotherapy
        - Assertive community treatment
        - Cognitive behavioural therapy
        - Dialectical behavioural therapy
        - Motivational interviewing
        - Multimodal behavioural therapy
        - Therapeutic communities
    - Medication (e.g., opioid or other substance replacement therapy)
    - Additional supports following treatment
- Length of time of treatment program
- 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)
- Financing treatment models
    - Public payment
    - Private payment
    - Mixed public private payment
- 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
    - Indigenous peoples
    - Black people, and other people of colour (i.e., Asian, Pacific Islanders, Latinx)
    - 2SLGBTQI+
- Outcomes

- Health outcomes
- Patient experience
- Provider experience
- Cost

What we found

We identified 43 evidence documents relevant to the question, of which we deemed 34 to be highly relevant, eight of medium relevance and one of low relevance. The highly relevant evidence documents include 24 evidence syntheses and 10 single studies.

In addition, three recently produced contextualized-evidence products may provide complementary insights:

- one rapid synthesis on involuntary substance-use treatment for adults, which addresses similar populations (e.g., those with recurrent substance use) and provides insights into inpatient care
- one rapid synthesis on pharmacist-delivered interventions for substance use, which provides insights into outpatient community-based care
- one rapid evidence profile on psychedelic-assisted psychotherapy, which provides insights into treatment-resistant mental health conditions that are frequently co-occurring with complex substance use.

Coverage by and gaps in existing evidence syntheses

The included evidence primarily addressed the use of opioids and alcohol. The included evidence documents use the term substance use to refer to individuals who use drugs or alcohol in any quantity, while the term substance-use disorder is defined according to the DSM-5, which combines the categories of substance abuse and substance dependence into a single measure on a continuum from mild to severe. Included evidence documents rarely used the term repeat treatment and instead referred to individuals as being treatment resistant or treatment refractory. To be categorized as treatment resistant or refractory requires an individual to have received previous substance-use treatment including psychotherapy and medication-assisted therapies for between six and 12 months and to have continued using substances (beyond those prescribed as part of medication-assisted therapies) throughout and following treatment. Given the relatively sparse literature, we have also included evidence syntheses that address the residential treatment and treatment for alcohol use disorder more generally, which were of particular interest to the requestor.

Despite the relatively high rates of comorbidity, only one recent high-quality evidence synthesis, five recent medium-quality evidence syntheses, one recent low-quality evidence synthesis and two single studies addressed co-occurring mental health conditions.(3-11)

Similarly, we identified relatively few documents that examined models of care specifically for this population. This includes one recent high-quality and one recent medium-quality evidence synthesis on the 12-step approach, one recent medium-quality evidence synthesis that included studies on each of the 12-step approach, stepped-care model and continuing-care model, and two single studies – one of which examined a stepped-care model while the other examined continuing care following inpatient treatment.(2; 5; 6; 8; 12) The remaining highly relevant evidence documents examined individual or combined program elements including psychotherapy (i.e., cognitive behavioural therapy, contingency management, motivational interviewing and therapeutic communities) and medication-assisted therapies. We also identified two recent medium-quality evidence syntheses and one single study examining deep-brain stimulation and one recent low-quality evidence synthesis examining non-invasive brain stimulation.(13-16)

Evidence documents addressed both inpatient and outpatient treatment settings. No evidence documents directly addressed the financing of treatment models, but two single studies examined cost-effectiveness using public willingness to pay thresholds for cost per quality-adjusted life year.(17; 18)

For priority populations, one recent medium-quality evidence synthesis and one single study included Veterans.(8; 19). One recent medium-quality evidence synthesis examined the effectiveness of inpatient residential treatment for Black populations, other people of colour and 2SLGBTQI+ people.(10) One recent medium-quality evidence synthesis examined the effectiveness of residential and community-based treatment on Indigenous populations,(20) while one recent medium-quality evidence synthesis and one single study focused on individuals who are homeless or marginally housed.(12)

Finally, with respect to outcomes, most findings related to health outcomes (frequently measured by reduction in substance use and improvements in quality of life) and care experiences (frequently measured by retention in treatment), and to a lesser extent, costs. We did not identify any outcomes related to provider experiences.

What existing syntheses and highly relevant single studies tell us about the effects on equity-centred quadruple-aim metrics

Included evidence documents addressed three of the four equity-centred quadruple-aim metrics – health outcomes, care experiences and to a lesser extent costs. We did not identify any evidence documents that included findings relevant to provider experiences. Below, we synthesize the included evidence by type of substance with additional insights available in Appendix 2, 3 and 4.

Multiple substances

With respect to health outcomes, one recent medium-quality evidence synthesis found positive effects for integrated treatment models that include both pharmacologic and psychologic treatment for those with comorbid mental illness and substance dependence (9)

Three medium-quality evidence syntheses found residential treatment to generally be effective for those with substance-use disorders.(9; 20; 21) Core components of residential treatment include 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. One of the medium-quality evidence syntheses focused on treatment for Indigenous populations and emphasized the importance of including and supporting elements of culturally appropriate care such as sweat lodge ceremonies, smudging, drumming and healing circles as well as traditional activities of fishing and hunting.(20)

One medium-quality evidence synthesis found insufficient evidence on post-discharge supports to facilitate transitions between inpatient and outpatient care. The synthesis suggested that some facilitators include leveraging existing partnerships between organizations, building trust and continuity across settings, and keeping open lines of communication.(22)

With respect to patient experience, one recent medium-quality evidence synthesis identified the effects of different contexts on the effectiveness of treatment for substance-use disorder. The synthesis found clients entering residential treatments had comparably better outcomes when they had a previous involvement with the justice system, had a high severity of substance use, and had positive pre-treatment relationships with friends and family.(10)

Alcohol

Two recent evidence syntheses (one high-quality and one low-quality) and two single studies (one of which was identified within a larger evidence synthesis) examined health outcomes related to psychotherapy. One recent high-quality evidence synthesis found alcoholics anonymous and 12-step facilitation are more effective than other clinical interventions in facilitating abstinence.(2) The recent low-quality evidence synthesis found dialectic behavioural

therapy reduced alcohol consumption among individuals with combined alcohol use disorder and border personality disorders. The two recent single studies reported positive health effects for motivational interviewing and from unilateral family therapy for treatment-resistant alcohol use, including reduction in alcohol consumption and improvements in psychological health.(3; 23)

Five recent evidence syntheses examined the effects of medication-assisted therapy on health outcomes. Two recent medium-quality evidence syntheses found mixed effects from ketamine-assisted psychotherapy for individuals with alcohol use disorder who have failed to respond to first-line agents.(24; 25) One of the evidence syntheses found it effectively reduced cravings and alcohol consumption, while the other was unable to report definitive conclusions.(24; 25) The remaining two evidence syntheses examined other types of medication. One recent high-quality review found acamprosate, topiramate and oral naltrexone reduced alcohol consumption among people with alcohol use disorder. (26) However, one recent high-quality and one recent medium-quality review suggested that there was inconclusive evidence on the effectiveness of initiation of naltrexone and gabapentin for inpatients.(27; 28)

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.(7)

With respect to care experiences, one recent medium-quality evidence synthesis identified perceived barriers to obtaining community-based pharmacotherapy for alcohol use disorder includes a lack of knowledge about services, complexity of prescribing, stigma, and medication accessibility including from formulary restrictions.(6)

Finally, one single study examined the use of a navigator following repeated admissions to a detox centre to support continuing care, and though no significant health effects were identified, the study found a $68 USD per month per patient saving.(29)

Opioids

For health outcomes, one single study examined a stepped-care model that began with treatment admission to an in-person treatment facility that draws on a wide range of disciplines and treatment approaches including psychotherapy and medication. The study found the approach was effective at improving psychiatric symptoms, self-care behaviour, verbal skills and disability among most of the admitted individuals with treatment-resistant dual-diagnoses.(12)

Two recent high-quality reviews found no comparative advantage of one psychosocial treatment over another to improve the mental health of chronic, treatment-resistant opioid and benzodiazepine users.(3; 30) One recent single study found providing adjunctive personalized psychosocial interventions, which include psychological change methods such as contingency management, alongside medication-assisted therapy was more effective among treatment-resistant patients than standard medication-assisted therapies alone.(17)

One recent single study found extended-release buprenorphine resulted in a reduction in emergency department visits and illicit opioid use among Veterans with chronic-opioid use.(19)

Two recent medium-quality evidence syntheses and one single study addressed the use of diacetylmorphine (or prescription heroin) for treatment-refractory heroin users. The two medium-quality evidence syntheses found supervised consumption of oral heroin may be effective as a maintenance treatment for those who have never injected heroin or who are seeking to change methods of consumption.(31; 32) The older single study examined supervised injection of prescription heroin and found no difference in health outcomes compared to injectable or oral methadone treatment, but found a greater decline in the use of additional illicit drugs compared to those using methadone.(33)

Two recent medium-quality evidence synthesis and one recent single study (which was based on a single case) found that deep brain stimulation may be effective in reducing the consumption of illicit drugs for treatment-refractory opioid users.(13; 15; 16) However, some adverse events were reported including dizziness, insomnia and weight gain, as well as a reported increase in substance use among three participants.(13) Similarly, 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.(14)

Findings related to care experiences were mostly focused on diacetylmorphine. One older medium-quality and one older low-quality evidence synthesis, as well as one older single study, found improved retention from supervised diacetylmorphine than methadone maintenance therapies for treatment-resistant opioid use.(18; 31; 34) 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.(31)

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.(34)

Finally, one older single study found high-threshold, high-dose methadone programs improved retention among individuals with treatment-resistant opioid-use and comorbid bipolar disorder.(5)

Two single studies examined costs. The first 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).(17) The second study is an older and found diacetylmorphine may be more cost-effective than methadone maintenance therapy among those with opioid-dependence refractory to treatment.(18)

Experiences from Five Eyes countries

For the jurisdictional scan, we looked at the federal level in each of the 'Five Eyes' countries – Australia, Canada, New Zealand, U.K. and the U.S. – to identify what repeat substance-use treatment services were covered for Veterans.

We were unable to find any mention of substance-use treatment services specific to repeat or treatment-resistant individuals. We were also unable to find any limitations on health insurance coverage for substance-use treatment related to previous use (e.g., where previous use would preclude the individual from using the program or service again). The exception to this was health insurance coverage limits in each jurisdiction for the number of services provided each year (e.g., 25 in-person counselling visits), which conceivably could be consumed based on repeat visits.

We only identified one mention of a specific model of treatment. In the U.S., Veteran's Affairs refers to continuing care as a service that is provided for Veterans that use substances following admission to an inpatient facility. Apart from this example, all countries referred to covering different program elements. All countries provided access and funding for both inpatient and outpatient psychological therapies and medication-assisted therapies. However, countries differ on whether there are specific program elements for Veterans or whether Veterans are expected to access care alongside the general population. Commonly identified program elements include short-term outpatient counselling, intensive outpatient treatment (e.g., day programs), residential live-in care, medically managed detoxification programs and drug substitution therapies.

Access to outpatient psychological therapies and day programs is provided through Veteran-specific programs such as Open Arms in Australia or Op Courage in the U.K. Access to medication-assisted therapy is frequently facilitated by a coordinator (or general practitioner) but delivered by general substance-use service providers in the public system. For example, in the U.K., Veteran's seeking access to outpatient medication-assisted therapy are referred by

their general practitioner to their local drug service. The exception to this is the U.S., where all services are provided within the Veterans Affairs health system.

Except for in Australia and the U.S., we did not identify specific inpatient substance-treatment programs for Veterans. Rather public, charitable and private options that provide intensive care including medically assisted detox, psychotherapy, and medication for co-occurring mental health conditions are available for Veterans to access in a similar manner to the general population. In some instances such as in Canada, additional funding (through the disability benefit) may be available. In Australia, the Department of Veterans Affairs will pay for private hospital admission for substance-use treatment in contracted hospitals. In the U.S., inpatient treatment is provided in Veterans Affairs operated hospitals.

Though not a specific program element, Veterans Affairs in the U.S. directly funds research into treatment-resistant mental health and substance use conditions that may provide select individuals with access to innovative treatments (such as ketamine use for treatment-resistant alcohol use) and if successful, may result in revising practice guidelines.

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