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SUMMARY WITH CRITICAL APPRAISAL

Treatment Programs for Opioid Use Disorders: A Review of Guidelines

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Authors: Casey Gray, Srabani Banerjee, Charlene Argáez

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

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Abbreviations

APS	American Pain Society
CPDD	College on Problems of Drug Dependence
CRD	Centre for Reviews and Dissemination
CRISM	Canadian Research Initiative in Substance Misuse
ECG	Electrocardiography
NICE	National Institute of Clinical Excellence
OUD	Opioid Use Disorder
WHO	World Health Organization

Context and Policy Issues

Opioids are a class of drugs that produce analgesic and central nervous system depressant effects that can also induce euphoria.[1,2] Opioids include natural opiates (e.g., morphine, codeine) and synthetic or semi-synthetic opioids (e.g., oxycodone, fentanyl, methadone) and can take the form of prescribed pain medications or illegally produced or obtained substances [2] Both prescribed and illegally obtained opioids can be associated with problematic use.[1,2] Opioid use disorder (OUD) is defined within the Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association as a problematic pattern of opioid use leading to clinically significant impairment or distress.[3] OUD is a chronic, relapsing type of substance use disorder characterized by periods of exacerbation and remission, with a persistent vulnerability for relapse [2,3]

OUD is associated with significantly increased rates of morbidity and mortality. According to Health Canada, the number of overdoses and deaths caused by opioids is on the rise and reflects a public health crisis.[1] Recent national data indicate there were at least 3,987 apparent opioid-related deaths in 2017, and of those 92% were accidental; this corresponds to a death rate of 10.9 per 100,000 population.[4] The rate of hospitalizations due to opioid poisoning increased 53 per cent between 2007-20018 and 2016-2017.[5] This increase in opioid-related harms underscores the need to identify evidence-based treatment approaches.

Options for the clinical management of opioid use disorder range along a treatment intensity spectrum.[6,7] Withdrawal management exists on the low intensity end of the treatment intensity spectrum; treatment options include tapered methadone or buprenorphine. Agonist therapies are moderate intensity treatments; treatment options include buprenorphine/naloxone or methadone. Specialist-led alternative approaches are high intensity treatments; treatment options include slow-release oral morphine. Including psychosocial or residential treatments can support each approach.[7] All options can be implemented with or without supportive therapies that include psychosocial and residential

treatments, and in conjunction with harm reduction strategies such as needle exchange programs.

The purpose of this review is to evaluate the guidelines for opioid addiction programs for the treatment of adults who are reducing or discontinuing opioids or undergoing opioid substitution therapy.

Research Question

What are the evidence-based guidelines regarding the use of opioid addiction programs for the treatment of adults who are reducing or discontinuing opioids or opioid substitution therapy?

Key Findings

Six evidence-based guidelines were identified regarding the use of programs for the treatment of opioid use disorders in adults. Included guidelines provide recommendations regarding the safety and clinical effectiveness of programs that address treatment, implementation, and adherence enhancement strategies. Two Canadian guidelines recommend initiating opioid agonist treatment with buprenorphine/naloxone where feasible as a first-line treatment option. This was a strong recommendation based on high quality evidence. Alternative strategies are recommended where buprenorphine/naloxone is not feasible, or where contraindications are identified. Psychosocial interventions aimed at reducing illicit drug use during detoxification and following completion include fostering social support (with the service provider, with peer groups and with existing network of family and carers) and use of contingency management.

Methods

Literature Search Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were added to limit the retrieval to guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2013 and August 2, 2018.

Selection Criteria and Methods

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

Table 1: Selection Criteria

Population	Adult patients who are reducing or discontinuing opioids or opioid substitution therapy
Intervention	Opioid addiction programs of any kind (e.g., pharmacological, psychosocial, peer-support)
Comparator	Not applicable
Outcome	Guidelines
Study Design	Evidence-based guidelines

Exclusion Criteria

Guidelines were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2013. Guidelines with unclear methodology were also excluded.

Critical Appraisal of Individual Studies

The included guidelines were critically appraised by one reviewer with the AGREE II instrument.[8] Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of each included study were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 113 citations were identified in the literature search. Following screening of titles and abstracts, 108 citations were excluded and five potentially relevant reports were retrieved for full-text review. Twenty one potentially relevant publications were retrieved from the grey literature search for full text review. Of these potentially relevant articles, 20 publications were excluded for various reasons, and six guideline publications met the inclusion criteria and were included in this report. Appendix 1 presents the PRISMA[9] flowchart of the study selection.

Summary of Study Characteristics

Additional details regarding the characteristics of included publications are provided in Appendix 2.

Study Design

Six evidence-based guidelines[6,7,10-13] were identified regarding the use of opioid addiction programs for the treatment of adults who are reducing or discontinuing opioids or opioid substitution therapy. All six guidelines were informed by systematic reviews of the evidence. The CRISM guideline represents an update of the BCCSU-CRISM guideline, and it is tailored from the provincial BC approach to a national approach.

Country of Origin

The Canadian Research Initiative in Substance Misuse (CRISM)[7] and British Columbia Centre on Substance Use (BCCSU)-CRISM[6] guidelines were published in Canada in 2018 and 2017, respectively. The American Pain Society – College on Problems of Drug Dependence (APS-CPDD) guidelines[10] were produced in the United States (US) and

published in 2014. The World Health Organization (WHO) guidelines[11] were released in 2014 in Geneva, Switzerland as international guidelines. The two National Institute for Health and Care Excellence (NICE) guidelines[12,13] were originally published in the United Kingdom (UK) in 2007 and revised in 2016 and 2014.

Patient Population

All six included guidelines provide recommendations for the treatment of adults with OUD.[6,7,10-13] Two guidelines were developed specifically for a particular population; the APS-CPDD guideline applies to individuals seeking methadone treatment in licensed treatment centres and the WHO guideline applies to those who are pregnant or postnatal.[10,11] Overall, the population of interest for the CRISM, BCCSU-CRISM and NICE guidelines is general, although they include recommendations for specific sub-populations (e.g., one NICE (psychosocial) guideline includes recommendations for individuals in prison or detention centres).[6,7,12,13]

Interventions

Recommendations regarding the following interventions are made: patient screening procedures,[10,11] patient education and support,[10,12] and treatments (e.g., oral agonist and antagonist pharmacotherapies, withdrawal management strategies, psychosocial treatment interventions and supports, and residential treatment).[7]

Outcomes

The primary outcome of interest for the APS-CPDD guidelines is safety.[10] The CRISM, BCCSD-CRISM, WHO and NICE (2014 and 2016) guidelines target clinical effectiveness (i.e., healthy outcomes for pregnant people,[11] engagement in treatment,[13] reduction/ abstinence in use of drugs,[12,13] reduced risk of relapse,[13] completion of treatment,[12] improvement in entry rate for naltrexone maintenance,[12] use of other drugs,[12] and severity of withdrawal[12]).

Summary of Critical Appraisal

The six evidence-based guidelines[6,7,10-13] were assessed using the AGREE II tool. All included guidelines were of relatively high quality, however there were limitations. Strengths of the guidelines are the overall objectives and populations to whom the guidelines apply are specifically described; guideline development groups included individuals from all relevant professional groups; the target users of the guidelines are clearly defined; systematic methods were used to search for evidence (2 guidelines included structured literature reviews with systematic methods,[6,7] 4 included systematic reviews[10-13]); the criteria for selecting the evidence, the strengths and limitations of the body of evidence, and the methods for formulating the recommendations are clearly described; the health benefits, side effects, and risks have been considered in formulating the recommendations; there is an explicit link between the recommendations and the supporting evidence; the guideline was externally reviewed by experts prior to its publication; a procedure for updating the guideline is provided; the recommendations are specific and unambiguous; the different options for management of the condition or health issue are clearly presented; competing interests of guideline development group members have been recorded. These features may increase the reliability of the recommendations as they demonstrate sound methodology and make these publications less prone to biases.

The limitations of the guidelines included: the CRISM,[7] BCCSU-CRISM,[6] and APS-CPDD[10] guideline development panels did not seek the views and preferences of the target population (patients, public, etc.) in the development of the guidelines.[6,7,10] While study quality was assessed in all guidelines, the two NICE guidelines did not present the strength of the recommendation or describe the quality of the evidence associated with each recommendation.[12,13] Regarding implementation, the APS-CPDD guideline does not include facilitators and barriers to its application, and advice and/or tools on how the recommendations can be put into practice are not provided.[10] Furthermore, the CRISM and the WHO guidelines include a note that tools will be produced, however it is unclear if this has been done.[7,11] While these implementation issues may make the guidelines more difficult to implement, they do not affect the trustworthiness of the recommendations. None of the included guidelines present monitoring or auditing criteria; all guidelines identify the funding body, however only the BCCSU-CRISM guideline explicitly reported that the views of the funding body have not influenced the content of the guideline,[6] although this is not expected to introduce bias.

Additional details regarding the strengths and limitations of included publications are provided in Appendix 3.

Summary of Findings

The detailed recommendations, the quality of evidence on which the recommendations were based, and the strength of recommendations can be found in Appendix 4.

Guidelines

Screening

The APS-CPDD, WHO, and both NICE guidelines include recommendations regarding the use of screening to establish opioid use; [10-13] however, the recommended assessments vary in the degree of comprehensiveness. The WHO guideline panel recommends that health care providers for people who are pregnant or postpartum ask their patients about their use of substances at each antenatal visit, prior to offering comprehensive and individualized care. [11] The NICE guidelines recommend that staff in mental health and criminal justice settings ask services users about illicit drug use, and that health care providers use biological testing as well as routine clinical questions to establish drug use I medical settings. [12,13] For patients seeking methadone therapy, the APS-CPDD panel recommends comprehensive medical and behavioural risk screening including use of electrocardiography (ECG) to identify those with an elevated risk for methadone-associated arrhythmia.[10] See Table 3 for detailed screening procedures.

Treatment

Regarding recommended treatment for opioid use disorder the two Canadian guidelines recommend opioid agonist treatment with buprenorphine-naloxone as the first-line treatment for OUD.[6,7] Methadone is recommended for those who respond poorly to buprenorphine-naloxone.[7] There are serious safety risks associated with use of methadone and the recommendations included in the APS-CPDD guideline are intended to represent measures that can be taken to promote safer use.[10] Primarily, the APS-CPDD panel recommends that patients using methadone should be monitored for sedation, for QTc interval prolongation (using ECG), and for common opioid adverse effects (via face-to-face or phone assessment with patients within 3 to 5 days after initiating methadone, and within 3 to 5 days after each dose increase.[10] The NICE psychosocial guidelines include

recommendations regarding the care of people who misuse drugs, including discussing whether to involve their families and carers in the treatment process and respecting their autonomy and privacy rights.[13]

Withdrawal Management

Withdrawal management (or detoxification) alone is not recommended due to poor safety and effectiveness.[6,7] This is consistent with the WHO guideline, which recommends that pregnant people with OUD continue or commence opioid maintenance therapy with methadone or buprenorphine rather than opioid detoxification, and refer those choosing detoxification to a medically supervised detoxification program. The NICE detoxification guideline identifies ccontraindications to detoxification as having a medical condition needing urgent treatment, being in police custody or short prison sentence, and presentation to acute or emergency setting for other conditions.

Adherence Support

Each guideline includes recommendations targeting improved adherence and engagement with the treatment program. These include recommendations regarding the support of informed decision making,[13] involving the patient in care decisions,[10,13] discussing social support,[13] routinely offering information and referral to take-home naloxone programs and other harm reduction services,[6] and the introduction of contingency management programs.[13] For example, the APS panel recommends that before initiating methadone treatment, health care providers speak with patients about the goals of therapy, availability of alternative therapies, plans for monitoring and adjusting doses, and potential adverse effects.

Additionally, the CRISM recommendations support using “a stepped and integrated care approach, in which treatment intensity is continually adjusted to accommodate individual patient needs and circumstances over time,” (page E247) and allows for moving between treatments as needed or chosen. As part of a stepped approach, NICE recommends contingency management programs, whereby incentives (e.g., privileges, vouchers for goods or services) are offered as a contingency for each negative drug test.[13] The NICE psychosocial guideline also includes the recommendation that the access to and choice of treatment should be the same whether treatment is being sought voluntarily or by legal requirement.[13] For people in prison, the NICE guideline includes recommendations that treatment options should be comparable to those available in the community and that a therapeutic community developed specifically to treat drug misuse in the prison environment may be appropriate for those with significant drug misuse problems.[13]

Recommendations regarding treatment simplification and intensification, alternative and adjunct treatment options, adjunct harm reduction strategies, approaches to avoid, follow-up, medication interactions, education and support, social support and engagement with family and carers, opportunistic brief interventions, contingency management, staff training, community and residential treatment, detoxification, rapid detoxification, procedures following relapse, comorbid conditions, and contraindications were also identified. A detailed list of the recommendations in presented in Appendix 4.

Limitations

The included guidelines were high quality (Appendix 3), however, there were limitations related to gaps in the recommendations. For instance, no recommendations specifically addressed treatment of Indigenous populations. As part of the Public Health Emergency

Response, the Government of Canada has committed to improving access to treatment for First Nations communities.[1,14] Evidence informed treatment strategies that are culturally appropriate are needed.

Additionally, very clear and specific recommendations regarding the use of methadone and monitoring of adults who are not pregnant were identified; however, recommendations for methadone treatment protocols for those who are pregnant were less detailed. New treatment options are currently being developed. As the field evolves, these guidelines will need to be constantly updated to incorporate new evidence.

Conclusions and Implications for Decision or Policy Making

Six high quality evidence-based guidelines were identified regarding the use of opioid addiction programs for the treatment of adults who are reducing or discontinuing opioids or opioid substitution therapy. Where assessed, recommendations tended to be strong and were based on very low- to moderate-quality evidence.

It was recommended across guidelines that patients with suspected opioid use disorder receive confirmatory screening. One guideline provided detailed criteria for screening patients with ECG to identify risk factors for cardiac arrhythmia (i.e., QTc interval prolongation) prior to initiating methadone and following methadone dose changes. Guidelines recommend that service providers should offer education and counselling to patients contemplating treatment, and that treatment should be individually tailored, based on patient preferences, health risks, experience with previous treatment, treatment goals, and psychological, social, and occupational needs. Ongoing support and monitoring are recommended to assess safety/adverse effects and adherence.

One guideline recommended that methadone or buprenorphine should be offered as the first-line treatment for opioid detoxification, with the decision based on patient preferences and risk factors. Another guideline recommended that methadone should not be offered, or only offered with modified protocol for patients with prolonged QTc interval. Ultra-rapid detoxification and accelerated detoxification should not be routinely offered, and sedation for ultra-rapid detoxification is not recommended. Psychosocial interventions are a low intensity treatment option that should normally include contingency management, behavioural couples' therapy, and cognitive behaviour therapy. Finally, guidelines recommend that treatment options should be widely accessible to treatment seeking Canadians, regardless of their context (e.g., rural areas, prison, health care settings).

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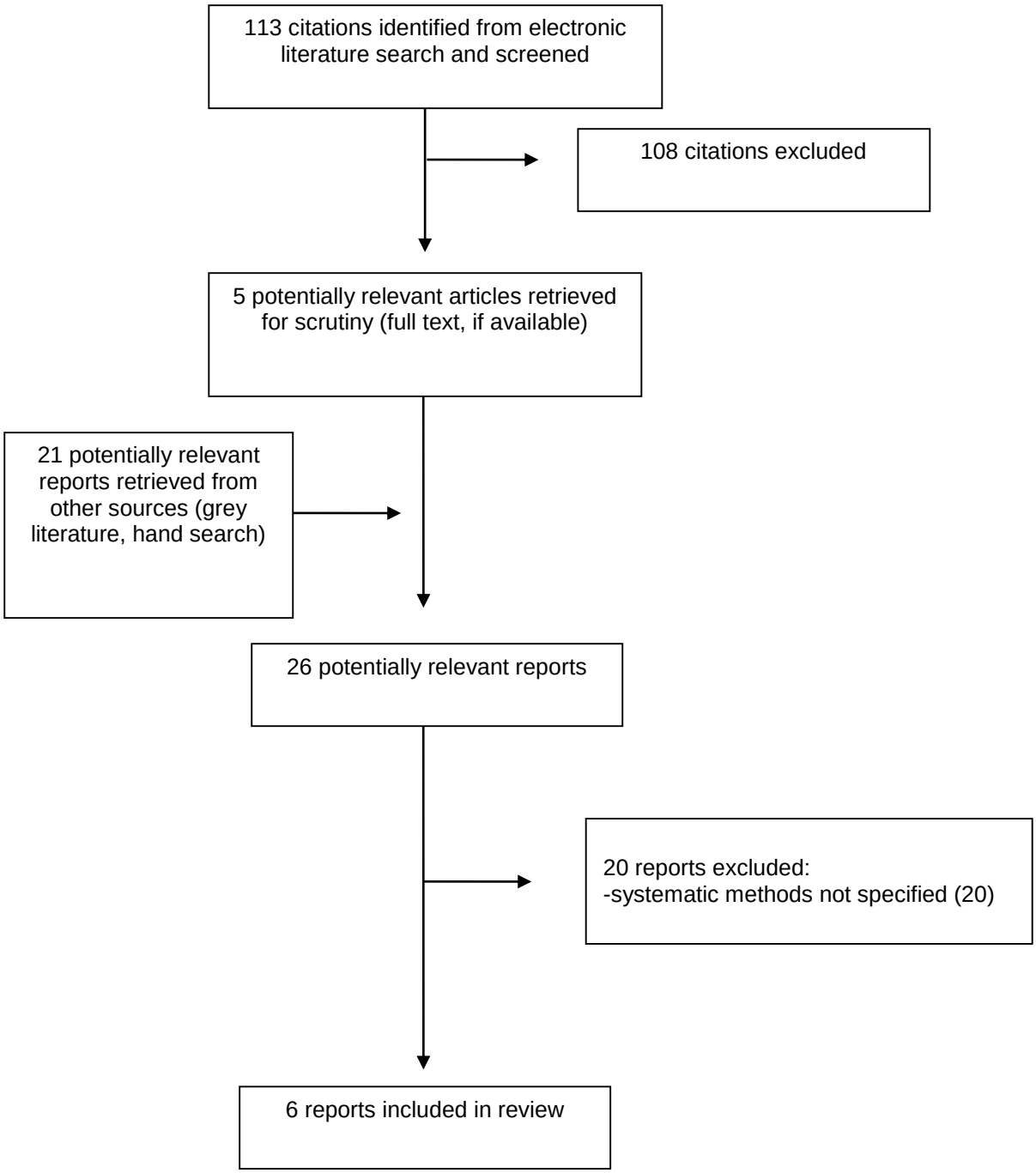
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 1: Characteristics of Included Guidelines

Intended Users, Target Population	Intervention and Practice Considered	Major Outcomes Considered	Evidence Collection, Selection, and Synthesis	Evidence Quality Assessment	Recommendations Development and Evaluation	Guideline Validation
CRISM, 2018[7]						
Canadian physicians, nurse practitioners, allied health care professionals, pharmacists, medical educators, clinical case managers, with or without specialized experience in addiction treatment; Policy makers and health care administrators; Adults with DSM-IV or DSM-5 confirmed opioid use disorder of any severity with primary use of illegal heroin or pharmaceutical opioid drugs.	Treatment approaches, including oral opioid agonist and antagonist pharmacotherapies, as well as withdrawal management strategies, psychosocial interventions, and peer-based support	Primary outcomes – retention in treatment, abstinence from or reduction in illicit opioid use; secondary outcomes – side effects, adverse events, morbidity and mortality	Systematic review was conducted; records were screened by at least 2 independent CRISM staff members for inclusion and compiled narrative evidence reviews.	GRADE	Recommendations were developed by a pan-Canadian review team through an iterative consensus process. The principal investigators drafted the recommendations and GRADE scores, revised by the review team in 2 rounds.	Externally reviewed by 2 external experts and 2 organizations representing people affected by opioid use disorders
BCCSU / CRISM, 2017[6]						
Health care providers; Policy makers	Medically-assisted withdrawal management/	Safety; effectiveness	A structured review is published within the guideline	GRADE	Draft recommendation statements were developed by	The guideline was circulated for external review and

Table 1: Characteristics of Included Guidelines

Intended Users, Target Population	Intervention and Practice Considered	Major Outcomes Considered	Evidence Collection, Selection, and Synthesis	Evidence Quality Assessment	Recommendations Development and Evaluation	Guideline Validation
and health care administrators; General population adolescent (12-17 years) and adult (18+ years) with moderate to severe opioid use	detoxification and referral to outpatient and/or residential treatment; residential treatment; Long-term opioid agonist therapy; Opioid antagonist medications; psychosocial interventions in conjunction with withdrawal management and opioid agonist medications; Harm reduction programs				committee. Consensus was sought and secured through group communication, email communication, and tracked document review and revision. Draft guidelines were circulated for review and consensus on the guideline content and recommendations was achieved during a face-to-face meeting A multi-stage Delphi process was used to rank recommendations; lowest ranked recommendations were eliminated. Consensus was achieved on the final list.	comment by relevant experts and stakeholders identified by the committee. Relevant revisions were incorporated by majority consensus.
APS/CPDD, 2014[10]						
Clinicians who prescribe methadone; Adults with opioid addiction, including pregnant women	Methadone for the treatment of opioid addiction	Safety	A systematic review was published in conjunction with the guideline to support the development of recommendations	GRADE	Draft recommendation statements were developed by the GDP. A multi-stage Delphi process was used to rank recommendations; lowest ranked recommendations were eliminated. Consensus was achieved on the final list.	Pre-release peer review was conducted by >20 clinical and scientific external peer reviewers. The final guideline was approved by the panel and the Boards of Directors for the American Pain Society and College on Problems of Drug Dependence approved the final Guideline

Table 1: Characteristics of Included Guidelines

Intended Users, Target Population	Intervention and Practice Considered	Major Outcomes Considered	Evidence Collection, Selection, and Synthesis	Evidence Quality Assessment	Recommendations Development and Evaluation	Guideline Validation
World Health Organization, 2014[11]						
Health care providers who provide prenatal, postnatal and infant care	Identification and management of substance use and substance disorders in pregnancy	Healthy outcomes for pregnant individuals and their fetus or infant	A systematic review was conducted by four investigators to identify recent Cochrane reviews or other high quality SRs. Where none existed, a de novo SR was conducted.	GRADE	Evidence profiles and GRADE tables were presented to the GDG. Final recommendations were formulated based on the evidence	Recommendations were reviewed by an external review group, revised and finalized by the GDG
NICE, 2016[13]						
Health care professionals; commissioners and providers; people who work in specialist residential and community-based treatment settings; people who work in prisons and criminal justice settings; People aged ≥16 years who misuse opioids, stimulants or cannabis and their families and carers (does not include pregnant people)	Psychosocial interventions in the context of properly coordinated care	Engagement in treatment, reduced injection risk behaviours, reduced incidence of blood-borne diseases, reduction/ abstinence in use of drugs, reduced risk of relapse, reduced crime	A systematic review was conducted to identify and synthesize relevant literature	Evidence profiles were created using GRADE; Study quality was evaluated using dimensions adapted from SIGN	Recommendations were developed by the GDG based on assessment of clinical and cost effectiveness evidence, with input from stakeholders	The draft guideline was posted on the NICE website for comment by registered stakeholders. The GRP reviewed the guideline and checked stakeholders comments were addressed. GDG finalized the recommendations.

Table 1: Characteristics of Included Guidelines

Intended Users, Target Population	Intervention and Practice Considered	Major Outcomes Considered	Evidence Collection, Selection, and Synthesis	Evidence Quality Assessment	Recommendations Development and Evaluation	Guideline Validation
NICE, 2014[12]						
Health care professionals; commissioners and providers; people who work in specialist residential and community-based treatment settings; people who work in prisons and criminal justice settings; People aged >16 years who misuse opioids and have been identified as suitable for a detoxification program	Opioid detoxification	Abstinence, completion of treatment, improvement in entry rate for naltrexone maintenance, use of other drugs, severity of withdrawal	A systematic review was conducted to identify and synthesize relevant literature	Study quality was evaluated using dimensions adapted from SIGN	NICE commissioned the National Collaborating Centre for Mental Health to develop this guideline. The Centre established a GDG, which reviewed the evidence and developed the recommendations. An independent GRP oversaw the development of the guideline	The draft guideline was posted on the NICE website for comment by registered stakeholders. The GRP reviewed the guideline and checked stakeholders comments were addressed. GDG finalized the recommendations

BCCSU = British Columbia Centre on Substance Use; CRISM = Canadian Research Initiative in Substance Misuse; DSM = Diagnostic and Statistics Manual; GRADE = The Grading of Recommendations Assessment, Development, and Evaluation; GDG = Guideline Development Group; GDP = Guideline Development Panel; GRP = Guideline Review Panel; SIGN = Scottish Intercollegiate Guidelines Network; WHO = World Health Organization

Table 2: Strengths and Limitations of Guidelines using AGREE II[8]

Item			Guideline					
			CRISM, 2018[7]	BCCSU - CRISM, 2017[6]	APS - CPDD, 2014[10]	WHO, 2014[11]	NICE, 2016[13]	NICE, 2014[12]
		Domain 1: Scope and Purpose						
1. The overall objective(s) of the guideline is (are) specifically described.			✓	✓	✓	✓	✓	✓
2. The health question(s) covered by the guideline is (are) specifically described.			✓	x	✓	✓	✓	✓
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.			✓	✓	✓	✓	✓	✓
		Domain 2: Stakeholder Involvement						
4. The guideline development group includes individuals from all relevant professional groups.			✓	✓	✓	✓	✓	✓
5. The views and preferences of the target population (patients, public, etc.) have been sought.			x	x	X	✓	✓	✓
6. The target users of the guideline are clearly defined.			✓	✓	✓	✓	✓	✓
		Domain 3: Rigour of Development						
7. Systematic methods were used to search for evidence.			✓	x	✓	✓	✓	✓
8. The criteria for selecting the evidence are clearly described.			✓	x	✓	✓	✓	✓
9. The strengths and limitations of the body of evidence are clearly described.			✓	✓	✓	✓	✓	✓
10. The methods for formulating the recommendations are clearly described.			✓	✓	✓	✓	✓	✓
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.			✓	✓	✓	✓	✓	✓
12. There is an explicit link between the recommendations and the supporting evidence.			✓	✓	✓	✓	✓	✓
13. The guideline has been externally reviewed by experts prior to its publication.			✓	✓	✓	✓	✓	✓

Table 2: Strengths and Limitations of Guidelines using AGREE II[8]

Item			Guideline			
14. A procedure for updating the guideline is provided.	✓	✓	✓	✓	✓	✓
Domain 4: Clarity of Presentation						
15. The recommendations are specific and unambiguous.	✓	✓	✓	✓	✓	✓
16. The different options for management of the condition or health issue are clearly presented.	✓	✓	✓	✓	✓	✓
17. Key recommendations are easily identifiable.	✓	✓	x	✓	X	X
Domain 5: Applicability						
18. The guideline describes facilitators and barriers to its application.	✓	✓	x	✓	✓	✓
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	x	✓	x	x	✓	✓
20. The potential resource implications of applying the recommendations have been considered.	✓	✓	x	✓	✓	✓
21. The guideline presents monitoring and/or auditing criteria.	x	x	X	X	X	X
Domain 6: Editorial Independence						
22. The views of the funding body have not influenced the content of the guideline.	unclear	✓	unclear	unclear	unclear	unclear
23. Competing interests of guideline development group members have been recorded and addressed.	✓	✓	✓	✓	✓	✓

Appendix 4: Main Study Findings and Authors' Conclusions

Table 3: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
CRISM, 2018[7]	
First- and second-line treatment options	
1. *"Initiate opioid agonist treatment with buprenorphine–naloxone whenever feasible, to reduce the risk of toxicity, morbidity and death, and to facilitate safer take-home dosing."* (pE250)	Strong recommendation, high quality evidence
2. *"For individuals responding poorly to buprenorphine–naloxone, consider transition to methadone treatment."* (pE250)	Strong recommendation, high quality evidence
3. *"Initiate opioid agonist treatment with methadone when treatment with buprenorphine–naloxone is not the preferred option."* (pE250)	Strong recommendation, high quality evidence
4. *"For individuals with a successful and sustained response to methadone who express a desire for treatment simplification, consider transition to buprenorphine–naloxone, because its superior safety profile allows for more routine take-home dosing and less frequent medical appointments."* (pE250)	Strong recommendation, moderate quality evidence
Alternative or adjunct treatment options	
5. *"In patients for whom first- and second-line treatment options are ineffective or contraindicated, opioid agonist treatment with slow-release oral morphine (initially prescribed as once-daily witnessed doses) can be considered. Slow-release oral morphine treatment should be prescribed only by physicians with a Section 56 exemption to prescribe methadone, or following consultation with an addiction practitioner experienced in opioid agonist treatment with slow-release oral morphine."* (pE250)	Strong recommendation, moderate quality evidence
6. *"Offering withdrawal management alone (i.e., detoxification without immediate transition to long-term addiction treatment) should be avoided, because this approach has been associated with increased rates of relapse, morbidity and death."* (pE250)	Strong recommendation, moderate quality evidence
7. *"When withdrawal management (without transition to opioid agonist treatment) is pursued, provide supervised slow (> 1 mo) opioid agonist taper (in an outpatient or residential treatment setting) rather than a rapid (<1 wk) taper. During opioid-assisted withdrawal management, patients should be transitioned to long-term addiction treatment† to help prevent relapse and associated health risks."* (pE250)	Strong recommendation, moderate quality evidence
8. *"For patients with a successful and sustained response to opioid agonist treatment who wish to discontinue treatment (i.e., desiring medication cessation), consider a slow taper approach (over months to years, depending on the patient). Ongoing addiction care should be considered on cessation of opioid use."* (pE250)	Strong recommendation, moderate quality evidence
9. *"Psychosocial treatment interventions and supports should be routinely offered but should not be viewed as a mandatory requirement for accessing opioid agonist treatment."* (pE250)	Strong recommendation, moderate quality evidence
10. *"Oral naltrexone can also be considered as an adjunct medication if cessation of opioid use is achieved."* (pE250)	Weak recommendation, low quality evidence
Adjunct harm-reduction strategies	

Table 3: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
11. *"Information and referrals to take-home naloxone programs and other harm reduction services (e.g., provision of clean drug paraphernalia), as well as other general health care services, should be routinely offered as part of standard care for opioid use disorders."* (pE250)	Strong recommendation, moderate quality evidence
BCCSU/CRISM, 2017 [6]	
Approaches to avoid	
1. *Withdrawal management alone (i.e., detoxification without immediate transition to long-term addiction treatment*) is not recommended, since this approach has been associated with elevated rates of relapse, HIV infection and overdose death. This includes rapid (< 1 week) inpatient tapers with methadone or buprenorphine/naloxone."* (p12)	Strong recommendation, moderate quality evidence
Possible first-line treatment options	
2. *"Initiate opioid agonist treatment with buprenorphine/naloxone whenever feasible to reduce toxicities and facilitate recovery through safer take-home dosing."* (p12)	Strong recommendation, high quality evidence
3. *Initiate opioid agonist treatment with methadone when treatment with buprenorphine/naloxone is not preferable (e.g., challenging induction)."* (p12)	Strong recommendation, high quality evidence
4. *If withdrawal management is pursued, for most patients, this can be provided more safely in an outpatient rather than inpatient setting. During withdrawal management, patients should be immediately transitioned to long-term addiction treatment* to assist in preventing relapse and associated harms. See also #9.* (p12)	Strong recommendation, moderate quality evidence
Adjunct or alternative treatment options	
5. *For individuals responding poorly to buprenorphine/naloxone, consider transition to methadone.* (p12)	Strong recommendation, high quality evidence
6. *"For individuals responding poorly to methadone, or with successful and sustained response to methadone desiring treatment simplification, consider transition to buprenorphine/naloxone."* (p12)	Strong recommendation, moderate quality evidence
7. *"For individuals with a successful and sustained response to agonist treatment desiring medication cessation, consider slow taper (e.g., 12 months). Transition to oral naltrexone could be considered upon cessation of opioids."* (p12)	Strong recommendation, moderate quality evidence
8. *"Psychosocial treatment interventions and supports should be routinely offered in conjunction with pharmacological treatment."* (p12)	Strong recommendation, moderate quality evidence
9. *"For patients wishing to avoid long-term opioid agonist treatment, provide supervised slow (> 1 month) outpatient or residential opioid agonist taper rather than rapid (< 1 week) inpatient opioid agonist taper. During withdrawal management, patients should be transitioned to long-term addiction treatment to prevent relapse and associated harms. Oral naltrexone can also be considered as an adjunct upon cessation of opioid use."* (p13)	Weak recommendation, low quality evidence
10. *"For patients who have been unsuccessful with first- and second-line treatment options, opioid agonist treatment with slow-release oral morphine (prescribed as once-daily witnessed doses) can be considered. Slow-release oral morphine should only be prescribed by experienced addiction practitioners who hold a Section 56 exemption to prescribe methadone or only after specialist consultation (e.g., RACE line).*	Strong recommendation, moderate quality evidence

Table 3: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
Practitioners who lack experience prescribing slow-release oral morphine for treatment of opioid use disorder, regardless of Section 56 exemption status, should consult with an experienced prescriber prior to initiating treatment." (p13)	
11. *"Information and referral to take-home naloxone programs and other harm reduction services should be routinely offered as part of standard care for opioid use disorder."* (p13)	Strong recommendation, moderate quality evidence
WHO, 2014[11]	
1. "*Health-care providers should ask all pregnant women about their use of alcohol and other substances (past and present) as early as possible in the pregnancy and at every antenatal visit*." (pxii)	Strong recommendation, low quality evidence
2. "*Health-care providers should offer a brief intervention to all pregnant women using alcohol or drugs*." (pxii)	Strong recommendation, low quality evidence
3. *"Health-care providers managing pregnant or postpartum women with alcohol or other substance use disorders should offer comprehensive assessment and individualized care."* **(pxii)**	Conditional recommendation, very low quality evidence
4. *"Health-care providers should, at the earliest opportunity, advise pregnant women dependent on alcohol or drugs to cease their alcohol or drug use and offer, or refer to, detoxification services under medical supervision where necessary and applicable."* **(p xii)**	Strong recommendation, very low quality evidence
5. *"Pregnant women dependent on opioids should be encouraged to use opioid maintenance treatment whenever available rather than to attempt opioid detoxification."* (pxii)	Strong recommendation, very low quality evidence
12. *"Pregnant patients with opioid dependence should be advised to continue or commence opioid maintenance therapy with either methadone or buprenorphine."* (pxii)	Strong recommendation, very low quality evidence
APS-CPDD, 2014[10]	
"When considering initiation of methadone, the panel recommends that clinicians perform an individualized medical and behavioral risk evaluation to assess risks and benefits of methadone, given methadone's specific pharmacologic properties and adverse effect profile." (p324)	*Strong recommendation, low-quality evidence*
"The panel recommends that clinicians educate and counsel patients prior to the first prescription of methadone about the indications for treatment and goals of therapy, availability of alternative therapies, and specific plans for monitoring therapy, adjusting doses, potential adverse effects associated with methadone, and methods for reducing the risk of potential adverse effects and managing them." (p324)	*Strong recommendation, low-quality evidence*
"The panel recommends that clinicians obtain an ECG prior to initiation of methadone in patients with risk factors for QTc interval prolongation, any prior ECG demonstrating a QTc >450 ms, or a history suggestive of prior ventricular arrhythmia. An ECG within the past 3 months with a QTc <450 ms in patients without new risk factors for QTc interval prolongation can be used for the baseline study." (p325)	*Strong recommendation, low-quality evidence*
"The panel recommends that clinicians consider obtaining an ECG prior to initiation of methadone in patients not known to be at higher risk for QTc interval prolongation; an ECG	*Weak recommendation, low-quality evidence*

Table 3: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
within the past year with a QTc <450 ms in patients without new risk factors for QTc interval prolongation can be used for the baseline study." (p325)	
"The panel recommends against use of methadone in patients with a baseline QTc interval >500 ms." (p327)	*Strong recommendation, low-quality evidence*
"The panel recommends that clinicians consider alternate opioids in patients with a baseline QTc interval $450 ms but<500 ms. If methadone is considered in a patient with a baseline QTc interval$450msbut<500ms, the clinician should evaluate for and correct reversible causes of QTc interval prolongation before initiating methadone." (p327)	*Weak recommendation, low-quality evidence*
"The panel recommends that clinicians consider buprenorphine as a treatment option for patients treated for opioid addiction who have risk factors for or known QTc interval prolongation when an agonist/partial agonist is indicated." (p327)	*Weak recommendation, moderate-quality evidence*
"The panel recommends that clinicians initiate methadone at low doses individualized based on the indication for treatment and prior opioid exposure status, titrate doses slowly, and monitor patients for sedation." (p327)	*Strong recommendation, moderate-quality evidence*
"The panel recommends that clinicians consider those patients previously prescribed methadone, but who have not currently taken opioids for 1 to 2 weeks, opioid-naıve for the purpose of methadone reinitiation." (p328)	*Strong recommendation, low-quality evidence*
"The panel recommends that for patients prescribed methadone, clinicians perform follow-up ECGs based on baseline ECG findings, methadone dose changes, and other risk factors for QTc interval prolongation." (p329)	*Strong recommendation, low-quality evidence*
"The panel recommends that clinicians switch methadone-treated adults with a QTc interval $500 ms to an alternative opioid or immediately reduce the methadone dose; in all such cases, the panel recommends that clinicians evaluate and correct reversible causes of QTc interval prolongation, and repeat the ECG after the methadone dose has been decreased." (p329)	*Strong recommendation, low-quality evidence*
"The panel recommends that clinicians consider switching methadone-treated adults with a QTc interval $450 ms but <500 ms to an alternative opioid or reducing the methadone dose. In patients in whom there are barriers to switching to alternative opioids, or who experience decreased treatment effectiveness with methadone dose reductions, the panel recommends that clinicians discuss with patients the potential risks of continued methadone. In all cases, the panel recommends that clinicians evaluate and correct reversible causes of QTc interval prolongation, and repeat the ECG after the methadone dose has been decreased." (p329)	*Strong recommendation, low-quality evidence*
"The panel recommends that patients receiving methadone be monitored for common opioid adverse effects and toxicities and that adverse effects management be considered part of routine therapy." (p330)	*Strong recommendation, moderate-quality evidence*
"The panel recommends face-to-face or phone assessment with patients to assess for adverse events within 3 to 5 days after initiating methadone, and within 3 to 5 days after each dose increase." (p330)	*Strong recommendation, low-quality evidence*

Table 3: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
"The panel recommends that clinicians obtain urine drug screens prior to initiating methadone and at regular intervals in patients prescribed methadone for opioid addiction." (p330)	*Strong recommendation, low quality evidence*
"The panel recommends that clinicians use methadone with care in patients using concomitant medications with potentially additive side effects or pharmacokinetic or pharmacodynamic interactions with methadone." (p330)	*Strong recommendation, low-quality evidence*
NICE, 2016[13]	
"People who misuse drugs should be given the same care, respect and privacy as any other person." (p40)	Not clear
"To enable people who misuse drugs to make informed decisions about their treatment and care, staff should explain options for abstinence-oriented, maintenance-oriented and harm-reduction interventions at the person's initial contact with services and at subsequent formal reviews." (p40)	Not clear
"When making an assessment and developing and agreeing a care plan, staff should consider the service user's: • *medical, psychological, social and occupational needs* • *history of drug use* • *experience of previous treatment, if any* • *goals in relation to his or her drug use* • *treatment preferences"* (p40)	Not clear
"Staff who are responsible for the delivery and monitoring of the agreed care plan should: • *establish and sustain a respectful and supportive relationship with the service user* • *help the service user to identify situations or states when he or she is vulnerable to drug misuse and to explore alternative coping strategies* • *ensure that all service users have full access to a wide range of services* • *ensure that maintaining the service user's engagement with services remains a major focus of the care plan* • *maintain effective collaboration with other care providers."* (p40)	Not clear
"Staff should discuss with people who misuse drugs whether to involve their families and carers in their assessment and treatment plans. However, staff should ensure that the service user's right to confidentiality is respected." (p74)	Not clear
"Staff should ask families and carers about, and discuss concerns regarding, the impact of drug misuse on themselves and other family members, including children. Staff should also: • *offer family members and carers an assessment of their personal, social and mental health needs* • *provide verbal and written information and advice on the impact of drug misuse on service users, families and carers."* (p74)	Not clear
"Routine clinical questions *6.2.4.1 Staff in mental health and criminal justice settings (in which drug misuse is known to be prevalent) should ask service users routinely about recent legal and illicit drug use. The questions should include whether they have used drugs and, if so:* • *of what type and method of administration*	Not clear

Table 3: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
• *in what quantity* • *how frequently."* (p80)	
"Routine clinical questions *In settings such as primary care, general hospitals and emergency departments, staff should consider asking people about recent drug use if they present with symptoms that suggest the possibility of drug misuse, for example:* • *acute chest pain in a young person* • *acute psychosis* • *mood and sleep disorders."* (p80)	Not clear
"*Biological tests* *Healthcare professionals should use biological testing (for example, of urine or oral fluid samples) as part of a comprehensive assessment of drug use, but they should not rely on it as the sole method of diagnosis and assessment."* (p80)	Not clear
"Opportunistic brief interventions focused on motivation should be offered to people in limited contact with drug services (for example, those attending a needle and syringe exchange or primary care settings) if concerns about drug misuse are identified by the service user or staff member. These interventions should: • *normally consist of two sessions each lasting 10–45 minutes* • *explore ambivalence about drug use and possible treatment, with the aim of increasing motivation to change behaviour, and provide nonjudgemental feedback."* (p98)	Not clear
"Opportunistic brief interventions focused on motivation should be offered to people not in contact with drug services (for example, in primary or secondary care settings, occupational health or tertiary education) if concerns about drug misuse are identified by the person or staff member. *These interventions should:* • *normally consist of two sessions each lasting 10–45 minutes* • *explore ambivalence about drug use and possible treatment, with the aim of increasing motivation to change behaviour, and provide nonjudgemental feedback."* (p98)	Not clear
"For people at risk of physical health problems (including transmittable diseases) resulting from their drug misuse, material incentives (for example, shopping vouchers of up to £10 in value) should be considered to encourage harm reduction. Incentives should be offered on a one-off basis or over a limited duration, contingent on concordance with or completion of each intervention, in particular for: • *hepatitis B/C and HIV testing* • *hepatitis B immunisation* • *tuberculosis testing."* (p105)	Not clear
"During routine contacts and opportunistically (for example, at needle and syringe exchanges), staff should provide information and advice to all people who misuse drugs about reducing exposure to blood-borne viruses. This should include advice on reducing sexual and injection risk behaviours. Staff should consider offering testing for blood-borne viruses." (p113)	Not clear
"Group-based psychoeducational interventions that give information about reducing exposure to blood-borne viruses and/or about reducing sexual and injection risk behaviours for people who misuse drugs should not be routinely provided." (p113)	Not clear
"Evidence-based psychological treatments (in particular, cognitive behavioural therapy) should be considered for the treatment of comorbid depression and anxiety disorders in line with	Not clear

Table 3: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
existing NICE guidance for people who misuse cannabis or stimulants, and for those who have achieved abstinence or are stabilised on opioid maintenance treatment." (p117)	
"Drug services should introduce contingency management programmes – as part of the phased implementation programme led by the NTA – to reduce illicit drug use, promote abstinence and/or promote engagement with services for people who primarily misuse stimulants." (p148)	Not clear
"Cognitive behavioural therapy and psychodynamic therapy focused on the treatment of drug misuse should not be offered routinely to people presenting for treatment of cannabis or stimulant misuse or those receiving opioid maintenance treatment." (p148)	Not clear
"Drug services should introduce contingency management programmes – as part of the phased implementation programme led by the NTA – to reduce illicit drug use and/or promote engagement with services for people receiving methadone maintenance treatment." (p177)	Not clear
"Contingency management aimed at reducing illicit drug use for people receiving methadone maintenance treatment or who primarily misuse stimulants should be based on the following principles. • *The programme should offer incentives (usually vouchers that can be exchanged for goods or services of the service user's choice, or privileges such as take-home methadone doses) contingent on each presentation of a drug-negative test (for example, free from cocaine or non-prescribed opioids).* • *If vouchers are used, they should have monetary values that start in the region of £2 and increase with each additional, continuous period of abstinence.* • *The frequency of screening should be set at three tests per week for the first 3 weeks, two tests per week for the next 3weeks, and one per week thereafter until stability is achieved.* • *Urinalysis should be the preferred method of testing but oral fluid tests may be considered as an alternative."* (p177)	Not clear
"Staff delivering contingency management programmes should ensure that: • *the target is agreed in collaboration with the service user* • *the incentives are provided in a timely and consistent manner* • *the service user fully understands the relationship between the treatment goal and the incentive schedule* • *the incentive is perceived to be reinforcing and supports a healthy/drugfree lifestyle*." **(**p177)	Not clear
"Drug services should ensure that as part of the introduction of contingency management, staff are trained and competent in appropriate near-patient testing methods and in the delivery of contingency management." (p177)	Not clear
"Contingency management should be introduced to drug services in the phased implementation programme led by the NTA, in which staff training and the development of service delivery systems are carefully evaluated. The outcome of this evaluation should be used to inform the full-scale implementation of contingency management." (p177)	Not clear
"Behavioural couples therapy should be considered for people who are in close contact with a non-drug-misusing partner and who present for treatment of stimulant or opioid misuse (including those who continue to use illicit drugs while receiving opioid maintenance treatment or after completing opioid detoxification). The intervention should: • *focus on the service user's drug misuse* • *consist of at least 12 weekly sessions."* (p178)	Not clear

Table 3: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
"All interventions for people who misuse drugs should be delivered by staff who are competent in delivering the intervention and who receive appropriate supervision." (p178)	Not clear
"For people receiving naltrexone maintenance treatment to help prevent relapse to opioid dependence, staff should consider offering: • *contingency management to all service users* • *behavioural couples therapy or behavioural family interventions to service users in close contact with a non-drug-misusing family member, carer or partner."* (p178)	Not clear
"Staff should routinely provide people who misuse drugs with information about self-help groups. These groups should normally be based on 12-step principles; for example, Narcotics Anonymous and Cocaine Anonymous." (p187)	Not clear
"If a person who misuses drugs has expressed an interest in attending a 12-step self-help group, staff should consider facilitating the person's initial contact with the group, for example by making the appointment, arranging transport, accompanying him or her to the first session and dealing with any concerns." (p187)	Not clear
"In order to reduce loss of contact when people who misuse drugs transfer between services, staff should ensure that there are clear and agreed plans to facilitate effective transfer." (p193)	Not clear
"Where the needs of families and carers of people who misuse drugs have been identified, staff should: • *offer guided self-help, typically consisting of a single session with the provision of written material* • *provide information about, and facilitate contact with, support groups, such as self-help groups specifically focused on addressing families' and carers' needs."* (p187)	Not clear
"Where the families of people who misuse drugs have not benefited, or are not likely to benefit, from guided self-help and/or support groups and continue to have significant problems, staff should consider offering individual family meetings. These should: • *provide information and education about drug misuse* • *help to identify sources of stress related to drug misuse* • *explore and promote effective coping behaviours* • *normally consist of at least five weekly sessions."* (p187)	Not clear
"The same range of psychosocial interventions should be available in inpatient and residential settings as in community settings. These should normally include contingency management, behavioural couples therapy and cognitive behavioural therapy. Services should encourage and facilitate participation in self-help groups." (p207)	Not clear
"Residential treatment may be considered for people who are seeking abstinence and who have significant comorbid physical, mental health or social (for example, housing) problems. The person should have completed a residential or inpatient detoxification programme and have not benefited from previous community-based psychosocial treatment." (p207)	Not clear
"People who have relapsed to opioid use during or after treatment in an inpatient or residential setting should be offered an urgent assessment. Offering prompt access to alternative community, residential or inpatient support, including maintenance treatment, should be considered." (p217)	Not clear
"For people who misuse drugs, access to and choice of treatment should be the same whether they participate in treatment voluntarily or are legally required to do so." (p219)	Not clear

Table 3: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
"For people in prison who have drug misuse problems, treatment options should be comparable to those available in the community. Healthcare professionals should take into account additional considerations specific to the prison setting, which include: • *the length of sentence or remand period, and the possibility of unplanned release* • *risks of self-harm, death or post-release overdose".* (p224)	Not clear
"People in prison who have significant drug misuse problems may be considered for a therapeutic community developed for the specific purpose of treating drug misuse within the prison environment." (p224)	Not clear
"For people who have made an informed decision to remain abstinent after release from prison, residential treatment should be considered as part of an overall care plan." (p224)	Not clear
NICE, 2014[12]	
"Detoxification should be a readily available treatment option for people who are opioid dependent and have expressed an informed choice to become abstinent." (p10)	Not clear
"In order to obtain informed consent, staff should give detailed information to service users about detoxification and the associated risks, including: • *the physical and psychological aspects of opioid withdrawal, including the duration and intensity of symptoms, and how these may be managed* • *the use of non-pharmacological approaches to manage or cope with opioid withdrawal symptoms* • *the loss of opioid tolerance following detoxification, and the ensuing increased risk of overdose and death from illicit drug use that may be potentiated by the use of alcohol or benzodiazepines* • *the importance of continued support, as well as psychosocial and appropriate pharmacological interventions, to maintain abstinence, treat comorbid mental health problems and reduce the risk of adverse outcomes (including death)."* (p10)	Not clear
"Service users should be offered advice on aspects of lifestyle that require particular attention during opioid detoxification. These include: • *a balanced diet* • *adequate hydration* • *sleep hygiene* • *regular physical exercise"* (p10)	Not clear
"Staff who are responsible for the delivery and monitoring of a care plan should: • *develop and agree the plan with the service user* • *establish and sustain a respectful and supportive relationship with the service user* • *help the service user to identify situations or states when he or she is vulnerable to drug misuse and to explore alternative coping strategies* • *ensure that all service users have full access to a wide range of services* • *ensure that maintaining the service user's engagement with services remains a major focus of the care plan* • *review regularly the care plan of a service user receiving maintenance treatment to ascertain whether detoxification should be considered* • *maintain effective collaboration with other care providers."* (p10-11)	Not clear
"People who are opioid dependent and considering self-detoxification should be encouraged to seek detoxification in a structured treatment programme or, at a minimum, to maintain contact with a drug service" (p11)	Not clear

Table 3: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
"Service users considering opioid detoxification should be provided with information about self-help groups (such as 12-step groups) and support groups (such as the Alliance); staff should consider facilitating engagement with such services." (p11)	Not clear
"Staff should discuss with people who present for detoxification whether to involve their families and carers in their assessment and treatment plans. However, staff should ensure that the service user's right to confidentiality is respected." (p11)	Not clear
"In order to reduce loss of contact when people who misuse drugs transfer between services, staff should ensure that there are clear and agreed plans to facilitate effective transfer." (p11)	Not clear
"All interventions for people who misuse drugs should be delivered by staff who are competent in delivering the intervention and who receive appropriate supervision." (p11)	Not clear
"People who are opioid dependent should be given the same care, respect and privacy as any other person." (p11)	Not clear
"Staff should ask families and carers about, and discuss concerns regarding, the impact of drug misuse on themselves and other family members, including children. Staff should also: • *offer family members and carers an assessment of their personal, social and mental health needs* • *provide verbal and written information and advice on the impact of drug misuse on service users, families and carers* • *provide information about detoxification and the settings in which it may take place* • *provide information about self-help and support groups for families and carers."* (p12)	Not clear
"People presenting for opioid detoxification should be assessed to establish the presence and severity of opioid dependence, as well as misuse of and/or dependence on other substances, including alcohol, benzodiazepines and stimulants. As part of the assessment, healthcare professionals should: • *use urinalysis to aid identification of the use of opioids and other substances; consideration may also be given to other near-patient testing methods such as oral fluid and/or breath testing* • *clinically assess signs of opioid withdrawal where present (the use of formal rating scales may be considered as an adjunct to, but not a substitute for, clinical assessment)* • *take a history of drug and alcohol misuse and any treatment, including previous attempts at detoxification, for these problems* • *review current and previous physical and mental health problems, and any treatment for these* • *consider the risks of self-harm, loss of opioid tolerance and the misuse of drugs or alcohol as a response to opioid withdrawal symptoms* • *consider the person's current social and personal circumstances, including employment and financial status, living arrangements, social support and criminal activity* • *consider the impact of drug misuse on family members and any dependants* • *develop strategies to reduce the risk of relapse, taking into account the person's support network."* (p12-13)	Not clear
"If opioid dependence or tolerance is uncertain, healthcare professionals should, in addition to near-patient testing, use confirmatory laboratory tests. This is particularly important when: • *a young person first presents for opioid detoxification* • *a near-patient test result is inconsistent with clinical assessment*	Not clear

Table 3: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
• *complex patterns of drug misuse are suspected."* (p13**)**	
"Near-patient and confirmatory testing should be conducted by appropriately trained healthcare professionals in accordance with established standard operating and safety procedures." (p13)	Not clear
"Opioid detoxification should not be routinely offered to people: • *with a medical condition needing urgent treatment* • *in police custody, or serving a short prison sentence or a short period of remand; consideration should be given to treating opioid withdrawal symptoms with opioid agonist medication* • *who have presented to an acute or emergency setting; the primary emergency problem should be addressed and opioid withdrawal symptoms treated, with referral to further drug services as appropriate."* (p13)	Not clear
"For women who are opioid dependent during pregnancy, detoxification should only be undertaken with caution." (p13)	Not clear
"For people who are opioid dependent and have comorbid physical or mental health problems, these problems should be treated alongside the opioid dependence, in line with relevant NICE guidance where available." (p14)	Not clear
"If a person presenting for opioid detoxification also misuses alcohol, healthcare professionals should consider the following. • *If the person is not alcohol dependent, attempts should be made to address their alcohol misuse, because they may increase this as a response to opioid withdrawal symptoms, or substitute alcohol for their previous opioid misuse.* • *If the person is alcohol dependent, alcohol detoxification should be offered. This should be carried out before starting opioid detoxification in a community or prison setting, but may be carried out concurrently with opioid detoxification in an inpatient setting or with stabilisation in a community setting."* (p14)	Not clear
"If a person presenting for opioid detoxification is also benzodiazepine dependent, healthcare professionals should consider benzodiazepine detoxification. When deciding whether this should be carried out concurrently with, or separately from, opioid detoxification, healthcare professionals should take into account the person's preference and the severity of dependence for both substances." (p14)	Not clear
"Methadone or buprenorphine should be offered as the first-line treatment in opioid detoxification. When deciding between these medications, healthcare professionals should take into account: • *whether the service user is receiving maintenance treatment with methadone or buprenorphine; if so, opioid detoxification should normally be started with the same medication* • *the preference of the service user"* (p14)	Not clear
"Lofexidine may be considered for people: • *who have made an informed and clinically appropriate decision not to use methadone or buprenorphine for detoxification* • *who have made an informed and clinically appropriate decision to detoxify within a short time period* • *with mild or uncertain dependence (including young people)."* (p14-15)	Not clear
"Clonidine should not be used routinely in opioid detoxification." (p15)	Not clear

Table 3: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
"Dihydrocodeine should not be used routinely in opioid detoxification." (p15)	Not clear
"Opioid detoxification refers to the process by which the effects of opioid drugs are eliminated from dependent opioid users in a safe and effective manner, such that withdrawal symptoms are minimised. This should be an active process carried out following the joint decision of the service user and healthcare professional, with continued treatment, support and monitoring. Detoxification should not be confused with stabilisation or gradual dose reduction." (p15)	Not clear
"When determining the starting dose, duration and regimen (for example, linear or stepped) of opioid detoxification, healthcare professionals, in discussion with the service user, should take into account the: • *severity of dependence (particular caution should be exercised where there is uncertainty about dependence)* • *stability of the service user (including polydrug and alcohol use, and comorbid mental health problems)* • *pharmacology of the chosen detoxification medication and any adjunctive medication* • *setting in which detoxification is conducted."* (p15)	Not clear
"The duration of opioid detoxification should normally be up to 4 weeks in an inpatient/residential setting and up to 12 weeks in a community setting." (p15)	Not clear
"Ultra-rapid and rapid detoxification using precipitated withdrawal should not be routinely offered. This is because of the complex adjunctive medication and the high level of nursing and medical supervision required." (p16)	Not clear
"Ultra-rapid detoxification under general anaesthesia or heavy sedation (where the airway needs to be supported) must not be offered. This is because of the risk of serious adverse events, including death." (p16)	Not clear
"Rapid detoxification should only be considered for people who specifically request it, clearly understand the associated risks and are able to manage the adjunctive medication. In these circumstances, healthcare professionals should ensure during detoxification that: • *the service user is able to respond to verbal stimulation and maintain a patent airway adequate medical and nursing support is available to regularly monitor the service user's level of sedation and vital signs* • *staff have the competence to support airways."* (p17)	Not clear
"Accelerated detoxification, using opioid antagonists at lower doses to shorten detoxification, should not be routinely offered. This is because of the increased severity of withdrawal symptoms and the risks associated with the increased use of adjunctive medications." (p17)	Not clear
"When prescribing adjunctive medications during opioid detoxification, healthcare professionals should: • *only use them when clinically indicated, such as when agitation, nausea, insomnia, pain and/or diarrhoea are present* • *use the minimum effective dosage and number of drugs needed to manage symptoms* • *be alert to the risks of adjunctive medications, as well as interactions between them and with the opioid agonist."* (p17)	Not clear
"Healthcare professionals should be aware that medications used in opioid detoxification are open to risks of misuse and diversion in all settings (including prisons), and should consider: • *monitoring of medication concordance* • *methods of limiting the risk of diversion where necessary, including supervised consumption."* (p17)	Not clear

Table 3: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
"Staff should routinely offer a community-based programme to all service users considering opioid detoxification. Exceptions to this may include service users who: • *have not benefited from previous formal community-based detoxification* • *need medical and/or nursing care because of significant comorbid physical or mental health problems* • *require complex polydrug detoxification, for example concurrent detoxification from alcohol or benzodiazepines* • *are experiencing significant social problems that will limit the benefit of communitybased detoxification."* (p18)	Not clear
"Residential detoxification should normally only be considered for people who have significant comorbid physical or mental health problems, or who require concurrent detoxification from opioids and benzodiazepines or sequential detoxification from opioids and alcohol." (p18)	Not clear
"Residential detoxification may also be considered for people who have less severe levels of opioid dependence, for example those early in their drug-using career, or for people who would benefit significantly from a residential rehabilitation programme during and after detoxification." (p18)	Not clear
"Inpatient, rather than residential, detoxification should normally only be considered for people who need a high level of medical and/or nursing support because of significant and severe comorbid physical or mental health problems, or who need concurrent detoxification from alcohol or other drugs that requires a high level of medical and nursing expertise." (p18)	Not clear
"*Following successful opioid detoxification, and irrespective of the setting in which it was delivered, all service users should be offered continued treatment, support and monitoring designed to maintain abstinence. This should normally be for a period of at least 6 months."* (p18-19)	Not clear
"Community detoxification should normally include: • *prior stabilisation of opioid use through pharmacological treatment* • *effective coordination of care by specialist or competent primary practitioners* • *the provision of psychosocial interventions, where appropriate, during the stabilisation and maintenance phases"* (p19)	Not clear
"Inpatient and residential detoxification should be conducted with 24-hour medical and nursing support commensurate with the complexity of the service user's drug misuse and comorbid physical and mental health problems. Both pharmacological and psychosocial interventions should be available to support treatment of the drug misuse as well as other significant comorbid physical or mental health problems." (p19)	Not clear
"People in prison should have the same treatment options for opioid detoxification as people in the community. Healthcare professionals should take into account additional considerations specific to the prison setting, including: • *practical difficulties in assessing dependence and the associated risk of opioid toxicity early in treatment* • *length of sentence or remand period, and the possibility of unplanned release* • *risks of self-harm, death or post-release overdose."* (p19)	Not clear
"Contingency management aimed at reducing illicit drug use should be considered both during detoxification and for up to 3–6 months after completion of detoxification." (p20)	Not clear

Table 3: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
"Contingency management during and after detoxification should be based on the following principles. • *The programme should offer incentives (usually vouchers that can be exchanged for goods or services of the service user's choice, or privileges such as take-home methadone doses) contingent on each presentation of a drug-negative test (for example, free from cocaine or non-prescribed opioids).* • *If vouchers are used, they should have monetary values that start in the region of £2 and increase with each additional, continuous period of abstinence* • *The frequency of screening should be set at three tests per week for the first 3 weeks, two tests per week for the next 3 weeks, and one per week thereafter until stability is achieved.* • *Urinalysis should be the preferred method of testing but oral fluid tests may be considered as an alternative."* (p20-21)	Not clear
"Staff delivering contingency management programmes should ensure that: • *the target is agreed in collaboration with the service user* • *the incentives are provided in a timely and consistent manner* • *the service user fully understands the relationship between the treatment goal and the incentive schedule* • *the incentive is perceived to be reinforcing and supports a healthy/drug-free lifestyle."* (p 21**)**	Not clear
"Drug services should ensure that as part of the introduction of contingency management, staff are trained and competent in appropriate near-patient testing methods and in the delivery of contingency management."(p21)	Not clear
"Contingency management should be introduced to drug services in the phased implementation programme led by the National Treatment Agency for Substance Misuse (NTA), in which staff training and the development of service delivery systems are carefully evaluated. The outcome of this evaluation should be used to inform the full-scale implementation of contingency management." (p21)	Not clear

ECG = electrocardiogram; ms = millisecond; NICE = National Institute for Health and Care Excellence; NTA = National Treatment Agency; RACE = rapid access to consultative expertise

* "In this context, "addiction treatment" refers to continued care for opioid use disorder delivered by an experienced care provider, which could include pharmacological treatment (opioid agonist or antagonist treatment), evidence-based psychosocial treatment interventions (private or publicly-funded programs), residential treatment, or combinations of these treatments. In isolation, harm reduction services, low barrier housing and unstructured peer-based support would not be considered "addiction treatment." Opioid agonist therapy can be provided as an outpatient or when individuals are admitted to inpatient addiction treatment."[6] p12

Appendix 5: Additional References of Potential Interest

CADTH Reports

Strategies for the reduction or discontinuation of opioids: guidelines. Ottawa (ON): CADTH; 2017 Apr: https://cadth.ca/sites/default/files/pdf/htis/2017/RB1078%20-%20Opioid%20Tapering%20Final.pdf Accessed 2018 Aug.

Funding and management of Naloxone programs in Canada. Ottawa (ON): CADTH; 2018 Mar: https://cadth.ca/funding-and-management-naloxone-programs-canada-0 Accessed 2018 Aug 30.

Buprenorphine implant for the treatment of opioid use disorder. Ottawa (ON): CADTH; 2017 Mar: https://www.cadth.ca/dv/ieht/buprenorphine-implant-treatment-opioid-use-disorder Accessed 2018 Aug 30.

Canada's opioid crisis: delivering robust evidence to guide our response. Ottawa (ON): CADTH; 2017 May: https://www.cadth.ca/canadas-opioid-crisis-delivering-robust-evidence-guide-our-response Accessed 2018 Aug 30.

Opioid evidence bundle. Ottawa (ON): CADTH; 2018 Jul: https://www.cadth.ca/evidence-bundles/opioid-evidence-bundle *See:* Opioid use disorder/addiction treatment https://cadth.ca/evidence-bundles/opioid-evidence-bundle/browse-category#treatment Accessed 2018 Aug 30.

Treatment for opioid dependence: guidelines. Ottawa (ON): CADTH; 2012 Sep: https://cadth.ca/media/pdf/htis/sept-2012/RC0390%20Opioid%20Dependency%20Guidelines%20Final.pdf Accessed 2018 Aug 30.