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CADTH RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

Inpatient and Outpatient Treatment Programs for Substance Use Disorder: A Review of Clinical Effectiveness and Guidelines

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

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Context and Policy Issues

In 2012, members of an estimated 3.8% of Canadian households had a substance use disorder in the previous year,[1] and 31.8% of regular Canadian Forces had alcohol abuse or dependence in 2013.[2] Patients with substance use disorder can be treated with hospital- or residential-based programs (inpatient care), or with home- or community-based programs (outpatient care), with treatment options for both inpatient and outpatient care ranging from medication, to counseling (such as cognitive behavioural therapy, motivational enhancement therapy), and recovery support services. The comparative efficacy between inpatient and outpatient care programs for substance use disorders is not clear, and in Canada, referral to inpatient versus outpatient facilities may vary across jurisdictions and clinical practices.

This Rapid Response report aims to review the clinical effectiveness of inpatient and outpatient treatment programs for adults with substance use disorders involving prescription medications such as analgesics or non-prescription substances such as cocaine, opioids such as heroine, marijuana (cannabis), or alcohol. Evidence-based guidelines associated with inpatient and outpatient treatment programs in adults with substance use disorders will also be examined.

Research Questions

1. What is the clinical effectiveness of inpatient and outpatient treatment programs in adults with substance use disorders?

2. What are the evidence-based guidelines associated with inpatient and outpatients treatment programs in adults with substance use disorders?

Key Findings

For patients with alcohol use disorders, better detoxification completion and abstinence rates, and similar adverse event rates, were found in outpatient care compared to inpatient care in a couple of studies with short follow-up periods (one to two months). One study with a longer follow-up period found inpatients consumed less alcohol than outpatients in the year after entering treatment. In patients with severe alcohol dependence, data from one study found initial but decreasing benefit of inpatient over outpatient care across time in alcohol abstinence. For patients with substance use disorders, data from one study showed inpatients are more likely to complete treatment than outpatients. The small number of studies found and their heterogeneity in design and reported outcomes cautioned the interpretation of the findings.

The evidence-based guidelines from British Columbia Ministry of Health on opioids use disorder recommend that withdrawal management, if needed, can be provided more safely in an outpatient setting rather than in an inpatient setting in most patients For patients who wish to avoid long-term opioid agonist treatment, supervised slow (longer than one month) outpatient or residential opioid agonist taper can be provided rather than rapid (less than one week) inpatient opioid agonist taper.

Methods

A limited literature search was conducted on key resources including Ovid Medline, PsycINFO, PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases and a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies and guidelines. Major subject headings only were used for the non-randomized studies portion of the search. The search was limited to English language documents published from January 1, 2012 to October 5, 2017.

Rapid Response reports are organized so that the evidence for each research question is presented separately.

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	Adults 18 to 65 years with substance use disorder/addiction disorder (e.g., abuse of prescription medications or cocaine, heroin, cannabis, alcohol)
Intervention	Inpatient treatment programs specifically for substance use disorders; Outpatient treatment programs specifically for substance use disorders
Comparator	Q1: Inpatient treatment programs; Outpatient treatment programs; No treatment; Wait list Q2: No comparator
Outcomes	Q1: Clinical effectiveness and safety Q2: Guidelines
Study Designs	Heath technology assessments, systematic reviews, meta-analyses, RCTs, non-RCTs, evidence-based guidelines

RCT = randomized controlled trial.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications were already reported in the included SRs, or were published prior to 2012.

Critical Appraisal of Individual Studies

The included systematic review, clinical studies, and guidelines were assessed using the AMSTAR checklist,[3] Downs & Black[4] and AGREE II[5] checklists, respectively. 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 977 citations were identified in the literature search. Following screening of titles and abstracts, 962 citations were excluded and 15 potentially relevant reports from the electronic search were retrieved for full-text review. One potentially relevant publication was retrieved from the grey literature search. Of these potentially relevant articles, 11 publications were excluded for various reasons, while five publications (one systematic review [SR], three primary clinical studies, one guideline) met the inclusion criteria and were included in this report. Appendix 1 describes the PRISMA flowchart of the study selection.

Summary of Study Characteristics

The included narrative systematic review (SR)[6] included 22 studies on community detoxification for adult patients with alcohol dependence (AD) and/or alcohol withdrawal. Follow-up periods ranged from one to 12 months. Most included studies did not have a comparator; two studies compared inpatient to outpatient settings. Outcomes included detoxification completion rate (percentage of patients who completed the detoxification program) and effectiveness of the program on abstinence and drinking outcomes, using validated scales. The study was conducted in UK, India and the US.

The included clinical trials were randomized controlled (RCT),[7] longitudinal observational,[8] and retrospective observational[9] studies. The studies compared inpatient to outpatient care in adult patients with alcohol abuse[7,8] or substance use disorders.[9] Primary outcomes included abstinence (using self-reported questionnaires, confirmed by blood chemistry),[7] number of drinks per drinking day,[7] the amount of alcohol consumed in 12 months after treatment entry,[8] and treatment completion rate.[9] The studies were conducted in the US.

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

Characteristics of the included studies are detailed in Appendix 2.

Summary of Critical Appraisal

The included SR[6] had an a priori design provided, independent study selection and data extraction procedure in place, performed by two reviewers, a comprehensive literature search was performed, a list of included studies and study characteristics were provided, and conflicts of interest were stated for the authors of the review. The study did not perform meta-analysis due to heterogeneity in patient eligibility and reporting outcomes among the included studies, did not assess publication bias (rationale not provided) or quality of the included studies, which would caution the interpretation of the review conclusions; and a list of excluded studies was not provided.

The included studies[7-9] had clearly described hypotheses, method of selection from source population and representation of the study population (i.e., patients with high alcohol involvement), main outcomes, interventions, patient characteristics, and main findings. Estimates of random variability and actual probability values were provided. The RCT[7] included only patients with high alcohol involvement limiting the generalizability of the findings to patients with lower alcohol involvement. Randomization was done effectively and the research staff was blinded to participants' setting assignment. The longitudinal observational study had baseline patients characteristics that were clinically and statistically different in the two groups (such as age, alcohol consumption and symptoms at intake), leading to cautioned interpretation of the findings, and it is uncertain to have enough power to detect clinically important effects between groups (power calculation not performed).[8] The retrospective observational study had variable criteria and definitions of the main outcomes (e.g., for "successful completion") across programs.[9]

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

Details of the critical appraisal of the included studies are presented in Appendix 3.

Summary of Findings

1. *What is the clinical effectiveness of inpatient and outpatient treatment programs in adults with substance use disorders?*

The narrative review reported the effectiveness and safety of community detoxification on adults with alcohol dependence.[6] Comparative outcomes between outpatient care (community) and inpatient care were reported in two studies with short follow-up periods (one or two months). A better detoxification completion rate with outpatient care than inpatient care was found in one quasi-experimental study and one RCT. Outpatient care also led to better abstinence rates in one RCT and drinking outcomes in one quasi-experimental study. Drinking outcomes were not further specified but were categorized as "good", "improved", "unimproved", or "unknown"; the difference between "good" and "improved" was not reported. Statistical significance was not reported for any comparison. There were no differences found in safety outcomes such as visual hallucination, suicidality and seizure between the two treatments. The authors concluded that evidence supports the case for community detoxification in patients with alcohol dependence.

The RCT with longer term follow-up (up to 18 months) reported the comparative effectiveness of community detoxification and inpatient care on adults with high-severity alcohol use disorder.[7] It found a statistically significant advantage for inpatient treatment (followed by 6 months outpatient care) in the percentage of days abstinent (PDA) over outpatient care (plus an additional 6 months outpatient care) in the first

month post-treatment, but the advantage was reduced by month 6 when the difference was no longer significant. A considerable agreement was observed between self-reported outcomes and blood chemistry assessments (the odds of a negative blood index doubled with each 10% increase in PDA). Monthly point prevalence abstinence (PPA) (probability of complete abstinence per month) was also in favour of inpatient care at month 1 and at month 6. Inpatients experienced drinking reduction, as measured by number of drinks per drinking day, while outpatients did not. Large drinking reduction was observed among participants with low-severity alcohol use in both inpatient and outpatient care, while large drinking reduction was observed among high-severity alcohol use participants in inpatient care only. The authors concluded that the evidence found initial but decreasing benefit of inpatient over outpatient care across time.

The prospective study reported the comparative effectiveness of inpatient and outpatient care (patients lived at home and commuted to the hospital to attend treatment) on adults with alcohol use disorders.[8] The study found inpatients consumed significantly less alcohol in the year after entering treatment than outpatients as measured by the Graduated Frequency Scale questionnaire, and had significantly greater engagement with Alcohol Anonymous program than outpatients in the year after treatment. It is noteworthy that self-reporting measures for alcohol consumption are subjective.

The retrospective study reported the comparative effectiveness of inpatient and outpatient care (details not specified) on adults with substance use disorders (alcohol, cocaine, marijuana, opioids, methamphetamines).[9] The study found inpatients are three times more likely to complete treatment than outpatients.

2. *What are the evidence-based guidelines associated with inpatient and outpatients treatment programs in adults with substance use disorders?*

The evidence-based guidelines from British Columbia Ministry of Health on opioids use disorder[10] recommend:

"If withdrawal management is pursued, for most patients, this can be provided more safely in an outpatient rather than inpatient setting." (p 12) (Quality of evidence: moderate; Strength of recommendation: strong). The recommendation was based on evidence from Cochrane SRs on the use of medication such as methadone, buprenorphine and adrenergic agonists for the management of opioid withdrawal, and committee consensus that community-based outpatient withdrawal management should be offered. It was stated that outpatient treatment allows for an individualized approach to therapy and may be less disruptive to patients and their families than inpatient treatment.

"*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.*" (p 13) (Quality of evidence: low; Strength of recommendation: weak). The authors believe that the slow approach permits a slower, more flexible and individualized approach to tapered agonist reduction, and allows for dose adjustment and stabilization in case withdrawal symptoms occur.

The main findings of the included studies are presented in Appendix 4.

Limitations

Findings from the included narrative SR need to be interpreted with caution as data were from two studies with no quality assessment provided. Generalizability of the findings is limited in the trial that included only patients with high alcohol involvement; patients in both groups this trial had additional outpatient care, making the comparison between inpatient and outpatient treatment not pure. Differences in baseline patient characteristics in the two groups in another included trial may lead to biased interpretation of the findings. Evidence on substance use disorder was found in one study in which the authors agreed that differences in the main outcome definitions (i.e., "successful completion") varied across programs, which presented a limitation of this study.

Conclusions and Implications for Decision or Policy Making

For patients with alcohol use disorders, better detoxification completion and abstinence rates, and similar adverse event rates, were found in outpatient care compared to inpatient care in a couple of studies with short follow-up periods (one to two months). One study with a longer follow-up period found inpatients consumed less alcohol than outpatients in the year after entering treatment. This may be explained by the controlled environment of inpatient care that avoids the distractions that could be present in an outpatient care situation. In patients with severe alcohol dependence, data from one study found initial but decreasing benefit of inpatient over outpatient care across time in alcohol abstinence. For patients with substance use disorders, data from one study showed inpatients are more likely to complete treatment than outpatients. The small number of studies found and their heterogeneity in design and reported outcomes cautioned the interpretation of the findings.

The evidence-based guidelines from British Columbia Ministry of Health on opioids use disorder recommend that withdrawal management, if needed, can be provided more safely in an outpatient setting rather than in an inpatient setting in most patients. For patients who wish to avoid long-term opioid agonist treatment, supervised slow (longer than one month) outpatient or residential opioid agonist taper can be provided rather than rapid (less than one week) inpatient opioid agonist taper. The slow approach may permit a more flexible and individualized approach to tapered agonist reduction, which allows dose adjustment and stabilization in case withdrawal symptoms occur.

A systematic review on patients' preferences to treatment for substance use disorders found the majority of patients preferred outpatient treatment over inpatient treatment, though the reasons for this preference were not explored in this review.[11] This renders shared decision making an important process in the treatment of patients with substance use disorders. Development and implementation of a protocol for evaluation and treatment of patients requesting alcohol detoxification may be important to standardize the care and choice between inpatient versus outpatient treatment.[12]

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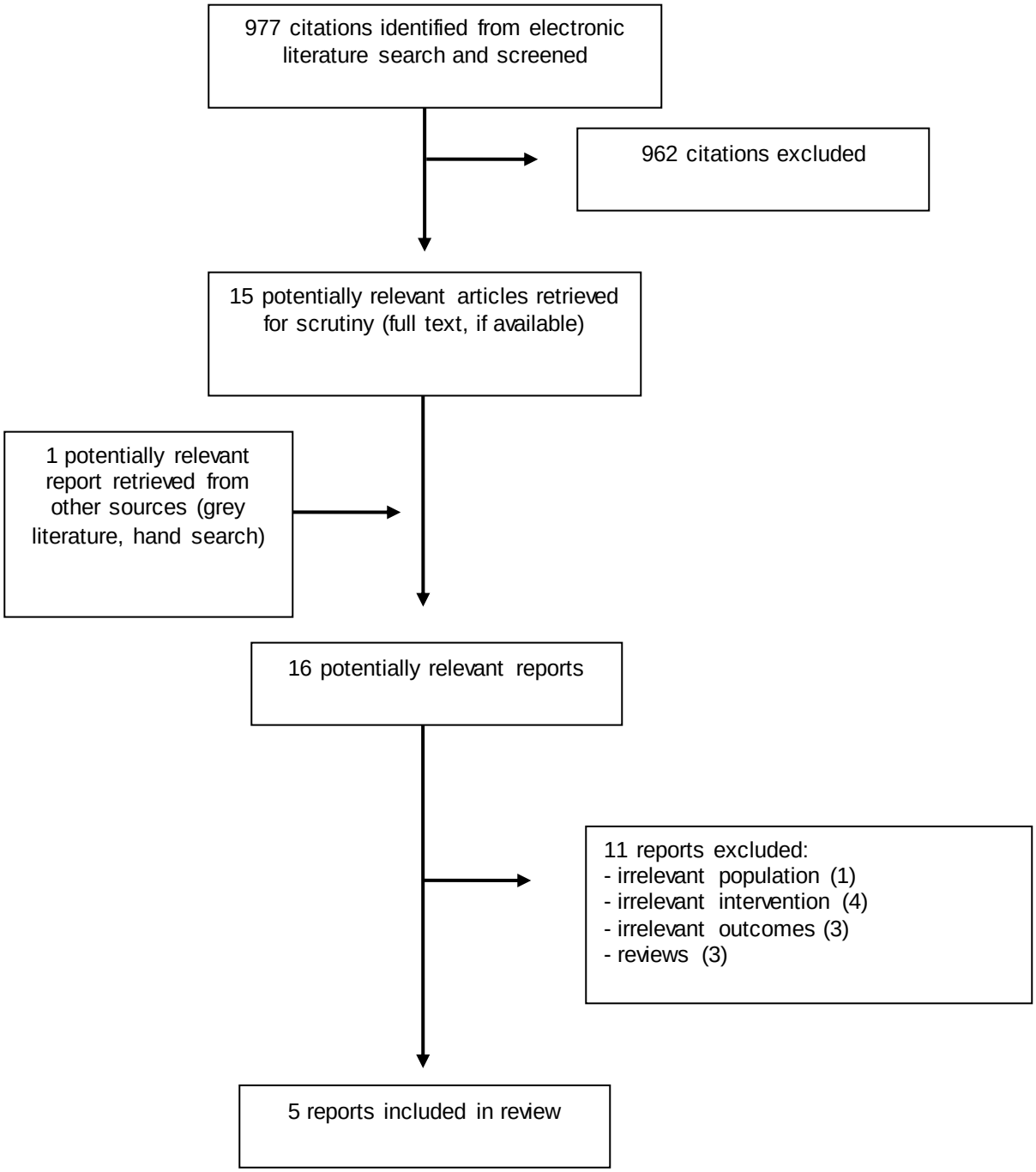
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Systematic Review

First Author, Year, Country	Objectives Literature Search Strategy	Inclusion Criteria	Exclusion Criteria	Studies included Main outcomes
Nadkarni,[o] 2017, India, UK, US	*"The aim of this systematic review is to synthesise the existing literature about the management of alcohol detoxification in the community to examine its effectiveness, safety, acceptability and feasibility"* (p 389) The following electronic databases were searched: Cochrane Library, Medline, EMBASE, PsycINFO,GlobalHealth and CINAHL	Studies with participants having AD (alcohol dependence) and/or alcohol withdrawal with or without comorbid physical/mental/substance use disorders were included. There were no restrictions on year of publication, gender and age of the participants. Only English language publications were included. Randomised controlled trials (RCTs), published audits, observational studies, case series and qualitative studies were included	Systematic reviews with or without meta-analyses and case reports were excluded.	22 studies (including 4 RCTs) Detoxification period: from 3 to 12days Detoxification completion rate Effectiveness: Abstinence, drinking outcomes (Severity of Alcohol Dependence Questionnaire, International Classification of Diseases 10th Revision Criteria, Michigan Alcoholism Screening Test, Severity of Withdrawal Symptom Checklist, Modified Selective Severity Assessment) Safety: detoxification-related adverse events

Table 3: Characteristics of Included Clinical Studies

First Author, Year, Country	Study Design Study Objectives	Interventions/Comparators	Patients	Main Outcomes
Rychtarik,[7] 2017, US	Randomized controlled trial *"In a tightly controlled, clinical research environment, Rychtarik et al. (2000) found that individuals with an alcohol use disorder (AUD) benefited more from inpatient (IP) than outpatient care, if they presented with high alcohol problem severity and/or low cognitive functioning. This study sought to (a) validate and extend these findings within the uncontrolled environment of a community-based treatment center and (b) test whether inpatients had fewer days of involuntary abstinence (e.g., incarcerations), controlling for differences in treatment expectancy across care settings"* (p 513)	Inpatient care(hospital-based) for 21 days plus 6 months of continuing outpatient care Outpatient care(community-based) for 21 days plus 6 months of continuing outpatient care Outpatient care: community-based health care network	Adult patients with alcohol use disorder (high severity and/or low cognitive function) 84 inpatients 92 outpatients	Primary outcomes: Percentage of days abstinent (PDA) Monthly point prevalence abstinence (PPA) Drinks per drinking day (DDD) Outcomes measured by self-reported questionnaire and blood chemistry testing Secondary outcome: Involuntary abstinence Treatment expectancy (6-item Feelings About Your Scheduled Treatment Scale) Assessed over 18 months.
Karriker-Jaffe,[8] 2017, US	Longitudinal observational study *"The current study aims were to examine effects of treatment type on alcohol consumption in the year after treatment intake and to test mediators of effects of treatment type on later alcohol use"* (p 1)	Inpatient care (hospital- or other residential-based) (median 42 days) Outpatient care (patients living at home and commute to the hospital to attend treatment) (median 16 sessions)	Adults with alcohol use disorder 167 inpatients 283 outpatients Inpatients had significantly more symptoms of problem drinking, higher alcohol consumption in the year prior to entering treatment than outpatients	Primary outcome: Amount of alcohol consumed in the 12 months after treatment entry (Graduated Frequency Scale) Secondary Outcome: Participation in Alcohol Anonymous program
Stahler,[9] 2016, US	Retrospective observational study *"This study investigates the impact of residential versus outpatient treatment setting on treatment completion"* (p 129)	Inpatient care (residential-based) (combination of both short ≤30days, and long term >30 days settings) Outpatient care	Adults with substance abuse (alcohol, cocaine, marijuana, opioids, metamphetamines) 49,141 inpatients 269,783 outpatients	Treatment completion rate

Table 4: Characteristics of Included Guidelines

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

Appendix 3: Critical Appraisal of Included Publications

Table 5: Summary of Critical Appraisal of Included Studies

First Author, Publication Year	Strengths	Limitations
Critical appraisal of included systematic review (AMSTAR[5])		
Nadkarni[6]	• a priori design provided • independent studies selection and data extraction procedure in place • comprehensive literature search performed • list of included studies, studies characteristics provided • conflict of interest stated	• assessment of publication bias not performed • list of excluded studies not provided • quality assessment of included studies not provided and used in formulating conclusions • heterogeneity across trials in patients' eligibility criteria and detoxification procedures precluded meta-analysis of the data
Critical appraisal of included clinical trial (Downs & Black[4])		
Rychtarik[7]	• randomized controlled trial • assessor blinded to patient treatment assignment. • hypothesis clearly described • method of selection from source population and representation described • loss to follow-up reported • main outcomes, interventions, patient characteristics, and main findings clearly described • estimates of random variability and actual probability values provided • study had sufficient power to detect a clinically important effect	• Both groups received additional outpatient care (the comparison is not pure between inpatient and outpatient care) • Patients got high risk alcohol use disorder before randomization, limiting the generalizability of the findings
Karriker-Jaffe[8]	• hypothesis clearly described • method of selection from source population and representation described • loss to follow-up reported • main outcomes, interventions, patient characteristics, and main findings clearly described • estimates of random variability and actual probability values provided	• Patients not randomized • Baseline characteristics different in the 2 groups • Unclear whether study had sufficient power to detect a clinically important effect
Stahler[9]	• hypothesis clearly described • method of selection from source population and representation described • loss to follow-up reported • main outcomes, interventions, patient	• Patients not randomized • Heterogeneity in definition of "successful completion" among individual programs

First Author, Publication Year	Strengths	Limitations
	characteristics, and main findings clearly described • estimates of random variability and actual probability values provided • study had sufficient power to detect a clinically important effect	
Critical appraisal of included guidelines (AGREE II[5])		
British Columbia Ministry of Health Guidelines[10]	• scope and purpose of the guidelines are clear • the recommendations are specific and unambiguous • the method for searching for and selecting the evidence are clear • methods used for formulating the recommendations are clearly described • health benefits, side effects and risks were stated in the recommendations • procedure for updating the guidelines provided • target users of the guideline are clearly defined	• unclear whether the guideline was piloted among target users • unclear whether patients' views and preferences were sought • potential cost implications of applying the recommendation not included

Appendix 4: Main Study Findings and Author's Conclusions

Table 6: Main Study Findings and Authors' Conclusions

Main Study Findings	Authors' Conclusions
Nadkarni[b] (Systematic Review)	
Detoxification completion rate: 90% for outpatient group, 78% for detoxification in the inpatient group (data from quasi-experimental study; follow-up 2months) 50% for outpatient group, 36.4% for the inpatient group (data from 1RCT; follow-up 1 month). Effectiveness Abstinence Outpatient group: 33.3%, inpatient group: 14.3% (data from 1 RCT; follow-up 1 month) Drinking outcomes Outpatient group: 45% good outcome, 17% improved, 28% unimproved, 10% unknown. Inpatient group: 31% good outcome, 3% improved, 44%unimproved, 19%unknown, 3% dead (data from 1 quasi-experimental study, follow-up 2 months) Safety: Visual hallucinations: no differences between outpatient and in-patient detoxification 10% vs 8% (data from 1 study) Suicidality: One patient with a schizophrenia diagnosis reported suicidality in outpatient detoxification(data from 1 study) Seizure: one case in each group (data from 1 study) No adverse events in outpatient detoxification group (data from 5 studies)	*"Although the current evidence base to some extent supports the case for community detoxification, there is a need for more randomised controlled trials testing the cost effectiveness of community detoxification in comparison with inpatient detoxification"* (p 389)
Rychtarik[f] (Clinical Trial)	
Primary outcomes: Percentage of (voluntary) days abstinent (PDA) (% per 30-day observation period) Inpatient: OR 3.40 at month1, OR 1.58 at month 6 Monthly PPA (probability of complete abstinence per month) Inpatient: OR 1.89 at month 1, OR 1.47 at month 6 DDD Inpatient: OR 1.17 at month 1, OR not reported at month 6 Large drinking reduction observed among low involvement participants in both inpatient or outpatient care Large drinking reduction observed among high involvement participants in inpatient care only Secondary outcome: involuntary abstinence Inpatient: OR 1.63 at month 1, OR not reported at month 6	*"To summarize, this study found support for (a) the initial but decreasing benefit of inpatient over outpatient care across time and (b) the validity of alcohol involvement as a client placement criterion for determinations of level of care decisions, at least with respect to alcohol consumption rates"* (p 522)
Karriker-Jaffe[o] (Clinical Trial)	
Inpatients consumed significantly less alcohol in the year after entering treatment than outpatients (absolute numbers not reported) (regression coefficient -0.95 [95% CI -1.67 to -0.23] *P* = 0.01) Inpatients had significantly greater engagement with Alcohol Anonymous program than outpatients in the year after treatment	*"Despite higher baseline problem severity and a shorter treatment duration, inpatient clients consumed less alcohol after treatment than outpatient clients"* (p 1)

Main Study Findings	Authors' Conclusions
Stahler[9] (Clinical Trial)	
Inpatients are 3 times more likely to complete treatment than outpatients (OR 3.014 [95% CI 2.943 to 3.086])	*"After controlling for other confounding factors, clients in residential treatment were nearly three times as likely as clients in outpatient treatment to complete treatment"* (p 129)
British Columbia Ministry of Health[10] (Evidence-based Guideline)	
"If withdrawal management is pursued, for most patients, this can be provided more safely in an outpatient rather than inpatient setting" (p 12) Quality of evidence: moderate (downgraded RCTs or upgraded observational studies) Strength of recommendation: strong (the recommendation can be adapted as policy in most situations) *"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."* (p 13) Quality of evidence: low (well-done observational studies with control groups) Strength of recommendation: weak (policy making will require substantial debates and involvement of many stakeholders)	Not applicable

95% CI = 95% confidence interval; DDD = drinks per drinking day; OR = odds ratio; PDA = Percentage of days abstinent; PPA = Monthly point prevalence abstinence; RCT= randomized controlled trial.