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Evidence Check

Supporting the update of the NSW Clinical Guidelines for Opioid Dependence Treatment (ODT)

An Evidence Check rapid review brokered by the Sax Institute
for the NSW Ministry of Health—November 2025

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November 2025

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Suggested Citation:

Suzanne Nielsen, Ali Cheetham, Tina Lam, Calvert Tisdale, Diki Tsering, Danni Teychenne, Veronica Delafosse, Peter Bragge. Supporting the update of the NSW Clinical Guidelines for Opioid Dependence Treatment (ODT): an Evidence Check rapid review brokered by the Sax Institute (www.saxinstitute.org.au) for the NSW Ministry of Health, 2025. doi:10.57022/gbra4260

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- The screening platform used (Covidence)[2] contains inbuilt AI functionality, which sorts citations by relevance (we do not use Covidence for data extraction)
- ChatGPT was used to assist in improving clarity of expression in sections of the report.

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Abbreviations

ACT: Australian Capital Territory

AE: Adverse event

AI: Artificial intelligence

AMSTAR 2: A Measurement Tool to Assess Systematic Reviews

aOR: Adjusted odds ratio

ASAM: American Society of Addiction Medicine

BPRU: Behavioural Pharmacology Research Unit

BUP: Buprenorphine

BUP/NAL: Buprenorphine/naloxone

CAMH: Centre for Addiction and Mental Health

CI: Confidence interval

CINA: Clinical Institute Narcotic Assessment

COVID-19: Coronavirus disease 2019

COWS: Clinical Opiate Withdrawal Scale

CPOP: Community Program for Opioid Pharmacotherapy

CRISM: Canadian Research Initiative in Substance Misuse

DATA: Drug Addiction Treatment Act

DOT: Directly observed therapy

DPS: Distriktspsykiatrisk poliklinikk (Norwegian; regional psychiatric centre)

DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders – 4th Edition – Text Revision

ED: Emergency department

FDA: Food and Drug Administration

GP: General practitioner

HCV: Hepatitis C virus

HIV: Human immunodeficiency virus

HR: Hazard ratio

I-AAM: Incentivised medication adherence and abstinence monitoring

ICB: Integrated care board

iOAT: Injectable opioid agonist treatment

ITT: Intention to treat

IVR: Interactive voice response

JBI: Joanna Briggs Institute

LAIB: Long-acting injectable buprenorphine

LAR: Legemiddel assistert rehabilitering (Norwegian; medication-assisted rehabilitation)

MATOD: Medication-assisted treatment for opioid dependence

mHealth: Mobile health

MMT: Methadone maintenance treatment

MOUD: Medications for opioid use disorder

NHMRC: National Health and Medical Research Council

NHS: National Health Service

NICE: National Institute for Health and Care Excellence

NIH: National Institutes of Health

NSW: New South Wales

OAT: Opioid agonist treatment

OBOT: Office-based opioid treatment

OD: Overdose

ODT: Opioid dependence treatment

OR: Odds ratio

OST: Opioid substitution therapy

OTP: Opioid treatment program

OUD: Opioid use disorder

PBS: Pharmaceutical Benefits Scheme

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses

QoL: Quality of life

QOTP: Queensland opioid treatment program

RCT: Randomised controlled trial

REMS: Risk evaluation and mitigation strategy

RR: Risk ratio

SAE: Serious adverse event

SAMHSA: Substance Abuse and Mental Health Services Administration

SANRA: Scale for the Assessment of Narrative Review Articles

SL: Sublingual

SOWS: Subjective Opiate Withdrawal Scale

SROM: Slow release oral morphine

TAB: Technology-assisted buprenorphine

TAU: Treatment as usual

TIP: Treatment improvement protocol

TA: Takeaway

TAD: Takeaway dose

TOPP: Tasmanian Opioid Pharmacotherapy Program Policy and Clinical Practice Standards

TSB: Tverrfaglig spesialisert rusbehandling (Norwegian; interdisciplinary specialised treatment)

UAE: United Arab Emirates

UDS: Urine drug screen

UDT: Urine drug test

UK: United Kingdom

US: United States

vDOT: Video directly observed therapy

Glossary of key terms

Community safety: Encompasses broader social outcomes related to diversion of doses to people who are not in treatment and accidental ingestion (e.g. by children).

Contextual aspects of service delivery: Factors related to the environment or structure of care that may moderate the relationship between dosing supervision and outcomes. These include setting (e.g. pharmacy, clinic, general practice), workforce (e.g. prescriber experience, pharmacist role), rurality, patient population characteristics, funding models, additional supports available (such as case management) and local regulatory frameworks. These are not always described in detail in studies and can vary over time in a given setting and between settings.

Contingent methadone takeaway dosing: Provision of methadone takeaways in a contingency management framework, where provision of takeaway doses is contingent on meeting a behavioural goal, such as regular attendance at counselling appointments or providing drug-free urine samples.

Methadone: A long-acting full opioid agonist used in opioid dependence treatment (ODT) for the management of opioid dependence. It is typically administered in liquid form and is subject to stricter supervision because of its overdose risk profile.

Number of takeaway doses: The quantity of unsupervised doses permitted within a defined time frame (e.g. per week). This may range from occasional single-day doses to multiple takeaways per week or per month.

Patient safety: Refers to the minimisation of adverse health outcomes for the individual receiving treatment. In the context of supervised versus unsupervised dosing, this includes risk of overdose, nonmedical use of medications or suboptimal adherence.

Sublingual buprenorphine: A partial opioid agonist used in opioid dependence treatment, available as monotherapy or in combination with naloxone. It is often taken as a daily dose, though it can be dosed on alternate days or every third day because of its long half-life and has a more favourable safety profile than methadone (e.g. has a ceiling on its respiratory depressant effects).

Supervised dosing*:* Refers to the administration of methadone or sublingual buprenorphine under direct observation by a healthcare professional (e.g. pharmacist, nurse or clinician), typically at a community pharmacy or clinic. Supervision is intended to ensure medication adherence, prevent diversion and monitor for adverse events during dosing.

Takeaway doses: Refers to individual doses dispensed for patient self-administration without observation, usually in the context some level of supervised dosing combined with provision of doses to be taken without direct supervision.

Treatment outcomes*:* Includes both clinical and psychosocial measures, such as opioid use, quality of life, psychosocial functioning, justice system involvement and health service usage. It may also include patient-reported outcomes such as treatment satisfaction or perceived autonomy.

Treatment retention: The duration of time a patient remains engaged in opioid dependence treatment without discontinuation or loss to follow-up. Retention is a widely used indicator of treatment effectiveness and a protective factor against opioid-related harms.

Unsupervised doses (sometimes referred to as 'takeaway doses'): Involves the dispensing of methadone or sublingual buprenorphine to patients for self-administration without direct observation.

Unsupervised treatment (including unsupervised induction): Refers to treatment or induction with no element of supervised dosing.

Key Messages

Unsupervised dosing can be safe and effective: Evidence from systematic reviews and primary studies show that unsupervised buprenorphine, including unsupervised induction, achieves outcomes comparable to supervised treatment, with clear benefits over no treatment and limited safety concerns.

Supervised dosing may not impact core outcomes: Limited systematic review evidence suggests that supervised dosing does not significantly improve retention, abstinence, or reduce mortality, suggesting that unsupervised approaches can be appropriate under certain conditions.

Methadone requires more caution: There is limited evidence on the safety of unsupervised methadone outside the COVID-19 context. However, during the pandemic, expanded takeaway dosing in patients that met defined criteria was generally not linked to safety concerns and sometimes linked to improved outcomes.

Contingent takeaway provision was linked to better outcomes: Older studies where takeaway doses were linked to indicators of stability (e.g. attendance or substance use measures) found this was associated with improved treatment outcomes. In contrast, noncontingent takeaways (i.e. not linked to stability) may increase risks.

Patient stability is considered important but is often poorly defined, with assessment practices unclear: Stability is widely cited as a criterion for takeaway dosing, yet clear definitions and practical assessment methods were not identified in most studies and guidelines. Research that described how clinicians assess suitability for takeaway doses or determine appropriate frequency was not identified, highlighting the need for expert judgement and clearer guidance on these aspects.

Some international guidelines allow more liberal unsupervised dosing: International guidelines also include additional medications not available in Australia (e.g. slow-release morphine, levomethadone, injectable hydromorphone).

Takeaway dosing improves patient experience: Reduced need for daily supervised dosing enhances autonomy, reduces stigma, and supports engagement in work and family life, with limited evidence of increases in diversion or misuse in the context of patients being assessed for suitability.

Considerations when interpreting findings: The rapid review methodology, limited timeframe, variability in study quality, and limited research on some aspects of the review limit the ability to draw firm conclusions on optimal dosing practices and assessment approaches.

Executive summary

Background

The supervised administration of opioid dependence treatments such as methadone and buprenorphine remains a central feature of opioid dependence treatment models in Australia. Given significant changes in both clinical practice and the treatment landscape—particularly the expansion of long-acting injectable buprenorphine and increased attention to patient-centred care—a timely and systematic review of the evidence for supervised versus unsupervised dosing is warranted. The aim of this Evidence Check rapid review was to identify, appraise and synthesise literature comparing supervised and unsupervised dosing of opioid dependence treatments with a focus on safety, effectiveness, retention and treatment experience. The review was designed to prioritise evidence applicable to the Australian context and inform recommendations for the revision of clinical guidelines and support evidence-based decision-making regarding dosing supervision within NSW. A secondary aim was to identify best practice across recent (published since 2020) Australian and comparable international guidelines for opioid dependence treatment.

Evidence Check questions

This review aimed to address the following questions and sub-questions:

Question 1: Are there differences in the effect of supervised versus unsupervised provision of methadone or sublingual buprenorphine as pharmacotherapy for opioid dependence on treatment retention, patient and community safety and other treatment outcomes?

Question 1a: *Does this effect differ by the number of takeaway doses provided?*

Question 1b: *Are there important contextual aspects of service delivery that are associated with these effects?*

Question 2: What is best practice clinical care (i.e. medication type and dosage) for people receiving pharmacotherapy[1] for opioid dependence in other Australian jurisdictions, and in countries with similar health system and socioeconomic characteristics?

[1] Including methadone, sublingual buprenorphine, long-acting injectable buprenorphine, oxycodone, morphine.

Summary of methods

For the first research question, we used a rapid systematic review approach. The key characteristic of this rapid review that distinguishes it from a full systematic review is that it focuses on studies published from 2020 onwards. However, this includes reviews and guidelines that will have identified, appraised and synthesised studies published before 2020. Additionally, a relevance-based search of the Google Scholar database (limited to the 100 most relevant articles) was used to capture key, highly cited publications prior to 2020 to ensure key studies conducted outside the search period could be considered, as we knew a larger body of research existed outside the review period. A protocol was registered on the Open Science Platform on 21 August 2025 [https://osf.io/pzf7t/]. We comprehensively searched four databases, with citations and full-text studies independently screened by two reviewers. We appraised the quality of reviews and primary studies using validated tools and used these to interpret study findings.

For the second research question, we conducted a limited online desktop review to identify and synthesise recent policy and clinical guidance on the pharmacological treatment of opioid dependence across selected jurisdictions. The review identified grey literature published since 2020 that is comparable in scope and intent to the *NSW Guidelines for the Treatment of Opioid Dependence*. We included publicly available policy documents, reports and clinical guidelines related to best practice pharmacological management of opioid dependence. Two relevant Australian guidelines published since 2020 were found and compared with guidelines from Canada, the UK, Norway and the US.

Key findings

Thirty-eight studies were eligible for the Evidence Check, comprising six systematic reviews and 32 primary studies. We identified an additional three ongoing studies.

A Cochrane systematic review did not find an effect of supervised dosing on retention, abstinence, diversion or mortality, noting most evidence was low to very low quality. Almost all participants were receiving methadone treatment, with a small number receiving sublingual buprenorphine. A second review compared observed buprenorphine induction with unsupervised induction, and found unsupervised induction was not associated with increased adverse events, increased substance use or lower treatment retention rates.

Four reviews that examined the impact of increased opioid dependence treatment takeaway dosing in the context of the COVID-19 pandemic generally found increased provision of unsupervised dosing during the pandemic was not associated with adverse safety outcomes (i.e. there was no change in overdose or mortality) and in some cases it was associated with improved clinical outcomes such as improved retention. Similarly, primary studies that were observational or used pre-post methods examined impacts of increased takeaway provisions during the COVID-19 pandemic and consistently found that expanded unsupervised (takeaway) dosing during COVID-19 and related policy changes did not have negative safety outcomes (and in some cases were associated with reduced overdose), and had either no effect or positive effects on clinical outcomes relating to substance use, retention and patient satisfaction.

Six studies conducted across diverse settings showed that when access to takeaway doses was conditional on patient behaviours (known as ‘contingent takeaway dosing’), providing takeaway doses was associated with improved outcomes. Risks were higher in models with noncontingent TA dosing. Taken together, the evidence suggests linking TA to treatment adherence, attendance or engagement supports better retention and lower substance use while noncontingent or routine provision of TA without assessing factors such as attendance or substance use does not appear to offer the same benefits and may increase risks relating to substance use and crime.

Unsupervised buprenorphine, compared with no treatment, was associated with clear benefits including reduced opioid use, less crime and better quality of life. When compared directly with supervised dosing, retention and substance use outcomes were generally similar. Overall, the findings suggest unsupervised dosing with buprenorphine can achieve equivalent outcomes to supervised dosing and may offer a way to increase treatment access. This extended to unsupervised buprenorphine induction, with no safety concerns identified.

For methadone, outcomes appear more sensitive to the degree of supervision and patient stability. For both medications, diversion and associated risks remain an important consideration. Of note, in the studies examined there were differences in the settings where methadone and buprenorphine were provided, and in the populations who received them, which may confound interpretation of the results. For example, in the US buprenorphine is often provided in primary care (or ‘office based’) settings whereas methadone is typically provided in clinics, although these differences are less distinct for research conducted in Australia. No study directly compared unsupervised methadone with unsupervised buprenorphine in a randomised design to assess the relative safety or effectiveness of unsupervised treatments with these two medications.

Recent studies of remote (e.g. video or smartphone) or electronic (e.g. electronic pillbox) supervision of opioid dependence treatment suggest these approaches are generally feasible, but most studies are pilots with these approaches appearing to be still in development.

Executive summary table		Safety			Effectiveness		
Type of paper	**Focus of paper**	**Poisoning/ overdose**	**Diversion**	**Retention**	**Substance use**	**Patient experience**	**Quality of life**
Systematic reviews Appendix 4	Unsupervised buprenorphine induction (compared with supervised) (n = 1) Supervised vs. unsupervised dosing (mainly methadone) (n = 1)	No effect on mortality(n = 1)	Not reported on in primary studies	No effect (n = 2)	No effect (n = 2)	Not reported on in primary studies	Not reported on in primary studies
	Increased takeaway doses during the COVID-19 pandemic (n = 4)	No effect on overdose/ mortality (n = 2)	Limited evidence, but no clear signal diversion was a concern with increased TAs (n = 2)	Not reported	No effect on substance use (n = 1); provider concern noted (n = 1)	↑with takeaways, and (n = 2); ↓ for patients who did not receive them (n = 1)	Not reported
Primary Studies Appendix 5	Contingent compared with non-contingent takeaway doses (n = 6)	Not reported	↑ with noncontingent takeaways only (n = 1)	↑ with contingent takeaways (n = 5)	↑ with noncontingent (n = 1), ↓ with contingent TA (n = 2); no change (n = 1)	Not reported	Not reported
	Unsupervised treatment vs. supervised or no treatment	No effect on mortality (n = 1)	Some diversion/injection of doses (n = 2); increased adherence with unsupervised+ pillbox (n = 1)	No (n = 2, buprenorphine) or mixed effect on retention (n = 1, methadone)	Similar to supervised (n = 1); reduced use with unsupervised compared with no treatment (n = 1)	High satisfaction with unsupervised treatment (n = 1)	Improved with unsupervised treatment (n = 2)
	Unsupervised buprenorphine induction compared with supervised (n = 4)	No safety issues identified	No comparator for interpretation	Better (n = 1)or same (n = 2) as with supervised induction	No clear comparison to assess	Satisfaction with supporting materials (n = 1)	Not reported
	Remote supervision (different modalities) (n = 6)	No overdoses reported during studies (n = 2)	Some evidence of tampering (n = 2); or high compliance (n = 1)	Improved adherence noted (n = 4)	No effect	Variable acceptability	Not reported
	Increased takeaway doses during the COVID-19 pandemic	No effect (n = 3) or reduced overdose (n = 2)	Not reported	Similar (n = 1) or ↑ (n = 3)	No change (n = 2), or increased use (n = 1)	Greater access, and satisfaction (n = 3)	Not reported
	Other: medication errors compared to unsupervised dosing (n = 1)	↑ medication errors with supervised dosing (n = 1)	Not reported	Not reported	Not reported	Not reported	Not reported

Evidence of benefits with unsupervised dosing/TA Evidence of concerns with unsupervised dosing/TA

A desktop scan of guidelines found the revised Queensland guidelines were consistent with the 2018 NSW guidelines in many respects. Points of difference include the introduction of a protocol for ‘micro-dosing’ of buprenorphine in Queensland (introduced in an addendum in 2023 in NSW). South Australia introduced a takeaway risk assessment process, with scoring to guide the level of unsupervised dosing.

Medications available in NSW were reflected in the international guidelines, namely oral methadone, sublingual buprenorphine (+/- naloxone) and long-acting injectable buprenorphine. These were typically considered first-line treatments. However, there were some nuances involved. For example, methadone may be indicated if the clinical outcomes with buprenorphine at high doses (e.g. > 24mg per day) were not optimal. In some cases, this was in the context of high-potency opioids being dominant in the drug market.

Other guidelines identified additional medications including slow-release oral morphine, methadone tablets, levomethadone, injectable hydromorphone and injectable diacetylmorphine. Other notable differences include lower maximum doses of 24 mg for sublingual buprenorphine in other countries (compared with a maximum of 32 mg typically seen in Australia).

Methadone recommended dose ranges are typically similar to common clinical practice in Australia (60 mg – 120 mg), though stronger recommendations are made regarding maximum doses or considering other (second-line) treatment options when this dose range does not provide good clinical outcomes. These alternative options are not currently described in NSW guidelines.

The international guidelines reviewed often enabled greater access to unsupervised dosing, with monthly collection of medications accessible to patients meeting certain levels of stability. Unsupervised buprenorphine was more commonly provided for 28–30 days, including from initiation of treatment. This contrasts with NSW guidelines, where provision of one-to-four weeks of unsupervised buprenorphine-naloxone dosing is only provided for those assessed as ‘low risk’. The provision of up to 28 days of unsupervised dosing is possible for methadone in the US after a period of stability, which far exceeds the current limits of unsupervised dosing in NSW. Federal law in the US has made these allowances permanent after they were introduced during the COVID era. These larger amounts of unsupervised doses were already possible and provided more routinely for buprenorphine with office-based treatment in the US. Second-line treatments such as Slow Release Oral Morphine (SROM) typically only allow unsupervised dosing in more exceptional circumstances.

Summary by key outcomes

Safety

Overdose and poisoning

Across all study types and settings, no studies reported increased overdose with provision, or increased provision of unsupervised doses of methadone or buprenorphine. Of note, community safety was less commonly assessed outside the context of the COVID-19 pandemic emergency orders.

Diversion

While not a dominant theme across the literature, some studies identified low levels of diversion. Diversion or tampering was most commonly reported in settings where patients who did not meet the criteria for stability were provided with unsupervised dosing, or where dosing was not linked specifically to such assessments.

Effectiveness

Retention

Across all study types and settings, the provision of increased unsupervised dosing or takeaways was associated with similar or improved retention in treatment, notably when takeaways were conditional on meeting treatment requirements.

Substance use

Most reviews and studies found providing unsupervised dosing or increased unsupervised dosing during the COVID-19 pandemic did not lead to changes in substance use. Where increased unsupervised dosing was linked to stability (such as attendance and substance use outcomes), decreased substance use was observed, and the opposite was seen with increased substance use when these factors were not considered with takeaway dosing.

Patient experience

Increased takeaways or unsupervised dosing was linked to positive patient experiences, greater treatment satisfaction and improved quality of life.

Guideline review

Australian and international guidelines generally align on first-line treatments (methadone and buprenorphine), though there are some nuances in terms of when methadone or buprenorphine may be preferred (e.g. depending on the local drug market context, patient preference and patient risk profile). Where buprenorphine sublingual formulations are discussed, most guidelines note buprenorphine-naloxone products are preferred over buprenorphine mono products. Innovations include micro-dosing protocols and takeaway risk assessment tools. Differences existed in terms of maximum doses and the extent of unsupervised dosing allowed,

with higher levels of unsupervised dosing in some international settings, especially for buprenorphine.

Some international guidelines allow broader treatment options beyond those commonly available in Australia, such as slow-release oral morphine, methadone tablets, levomethadone, and injectable hydromorphone and diacetylmorphine.

Limitations

This Evidence Check was constrained by a short timeline and focused on evidence from countries with treatment systems comparable to NSW, which may limit broader generalisability. Many included studies were observational, small, or conducted during the COVID-19 pandemic, and data were often inconsistently reported. Few studies specified the number of takeaway doses provided or described structured approaches for assessing takeaway suitability, limiting the ability to draw firm conclusions on these aspects of care. Patient-centred outcomes such as satisfaction and quality of life were also rarely reported.

Conclusion

In summary, the evidence indicates that supervision requirements in pharmacotherapy treatment for opioid dependence can be most effective when increased take-aways are linked to indicators of patient stability and treatment progress, such as attendance, engagement and substance use outcomes; and increasing unsupervised dosing among patients who met stability criteria during the COVID-19 pandemic supports that increased flexibility can be offered without comprising safety or treatment outcomes.

Takeaway dosing and unsupervised induction with buprenorphine achieves outcomes comparable to supervised dosing for safety, retention and substance use, while improving patient satisfaction and quality of life. For methadone, outcomes appear more sensitive to the degree of supervision, with better results observed when takeaway dosing is linked to indicators of treatment progress. These findings support the importance of clinical assessment to determine the level of supervision required to maintain safety while maximising treatment flexibility, support patient autonomy and strengthen the alignment of opioid dependence treatment with patient-centred practice.

Examining international practice offers further opportunity for increasing choice and effectiveness of treatment, including by considering additional pharmacotherapy treatment options.

Introduction

The supervised administration of opioid dependence treatments such as methadone and buprenorphine remains a central feature of treatment models in Australia. In NSW, the current Clinical Guidelines for the Treatment of Opioid Dependence[3] recommend supervised dosing during the initiation and stabilisation phases, with unsupervised or 'takeaway' doses permitted only under specific clinical conditions.

While the rationale for supervised dosing is grounded in safety concerns[4], some literature suggests that in some patients unsupervised dosing may be associated with comparable outcomes in retention and safety, and may reduce treatment burden stigma and barriers to access.[5] Moreover, the experience during the COVID-19 pandemic—with temporary regulatory flexibilities introduced to allow increased access to takeaway doses—demonstrated the potential for more flexible models of care without a corresponding rise in adverse events.[6,7] However, there has not been a recent synthesis of evidence. Existing systematic reviews, including a Cochrane review into supervised versus unsupervised dosing, highlight the paucity and low quality of evidence[8] and only include studies published up until 2016.

In NSW, opioid dependence treatment is provided across a diverse range of service settings. These include public clinics, general practice and community pharmacy. Variation in access to takeaway dosing across prescribers and sites may contribute to inequities in care and inconsistencies in risk assessment and management. Additionally, as the treatment population has evolved over time, there is a need to revisit the assumptions and practices underpinning supervised dosing. Given significant changes in both clinical practice and the treatment landscape—particularly the expansion of long-acting injectable buprenorphine and increased attention to patient-centred care—a review of the evidence about supervised versus unsupervised dosing is warranted to support evidence-based decision-making regarding dosing supervision within NSW.

Aims

The aim of this Evidence Check was to find, appraise and synthesise literature comparing supervised and unsupervised dosing of opioid dependence treatments with a focus on safety, effectiveness, retention and treatment experience. A secondary aim was to identify best practice in recent (published since 2020) Australian and comparable international guidelines for opioid dependence treatment.

To achieve these aims, we conducted a restricted review of the peer-reviewed literature to answer the following research questions and sub-questions:

Question 1: Are there differences in the effect of supervised versus unsupervised provision of methadone or sublingual buprenorphine as pharmacotherapy for opioid dependence on treatment retention, patient and community safety and other treatment outcomes?

Question 1a: *Does this effect differ by the number of takeaway doses provided?*

Question 1b: *Are there important contextual aspects of service delivery that are associated with these effects?*

Question 2: What is best practice clinical care (i.e. medication type and dosage) for people receiving pharmacotherapy[2] for opioid dependence in other Australian jurisdictions, and in countries with similar health system and socioeconomic characteristics?

Given the differing nature of the two research questions, different methods were employed to gather relevant evidence in relation to each. For clarity, the methods and results for each question are reported separately in the subsequent sections of this Evidence Check.

[2] Including methadone, sublingual buprenorphine, long-acting injectable buprenorphine, oxycodone, morphine.

Methods: Question 1

Methods for question 1, described below, were contained in a protocol registered on the Open Science Platform on 21 August 2025 [https://osf.io/pzf7t/].

We used a rapid systematic review approach to address this Evidence Check question. Rapid reviews bring together knowledge from published research using a systematic approach combined with techniques to enhance resource efficiency. The Cochrane Collaboration described these techniques as “speeding up the ways we plan, do, and/or share the results of conventional structured (systematic) reviews, by simplifying or omitting a variety of methods that should be clearly defined by the authors” [p. 3].[9]

Rapid reviews have evolved over the past 15 years to balance the need for comprehensiveness and rigour against the relatively short time lines of end-users such as policy makers.[10] We adhered to recommended practices in rapid reviews, namely thoughtful co-design of review parameters with knowledge users; limiting data extraction to the most important relevant areas pertaining to the research question; and using flexible searching techniques across at least two databases and with input from a specialist librarian.[9] Our approach was consistent with the PRISMA statement.[11]

The key characteristic of this Evidence Check rapid review that distinguishes it from a full systematic review is that it focuses on studies published from 2020 onwards. However, this includes reviews and guidelines that will have identified, appraised and synthesised studies published before 2020. Additionally, a relevance-based search of the Google Scholar database (limited to the 100 most relevant articles) was used to capture key / highly cited publications prior to 2020.

Rapid reviews offer a comprehensive summary of research in a defined time period and employ more robust techniques, which minimise bias. They satisfy standards for publication in a peer-reviewed journal but carry limitations associated with covering literature in a defined period. These are discussed in further detail in the Limitations section.

Search strategy

The search strategy was developed with the assistance of an experienced librarian. We searched four databases (MEDLINE (Ovid), Embase, Scopus and EBM Reviews: Cochrane Database of Systematic Reviews) for peer reviewed literature published between January 2020 and August 2025. This search was supplemented by a relevance-based search of Google Scholar (limited to the 100 most relevant articles) to capture key / highly cited publications prior to 2020 to ensure key studies conducted outside the search period were considered. A protocol

was registered on the Open Science Platform on 21 August 2025 [https://osf.io/pzf7t/]. See **Appendix 1** for full search strategies.

Study selection and screening

Citations were imported into Covidence, a web-based collaboration software platform that streamlines the production of systematic and other literature reviews.[2] Two reviewers independently screened titles / abstracts and full-text publications against the inclusion and exclusion criteria listed in **Table 1**. Disagreements were resolved by consensus, with the involvement of a third reviewer as required.

Table 1: Eligibility criteria

Inclusion criteria	Exclusion criteria
Study type	
• Original research reported in an evaluation or intervention study that assesses the effectiveness of an intervention or model of care for specified outcomes of interest, using either an experimental, quasi-experimental, pre/post study design, or observational design (levels II to IV on the NHMRC evidence hierarchy)	• Qualitative studies • Narrative studies and other non-systematic reviews • Grey literature
Population of interest	
• Opioid-dependent adults aged 18 years or older receiving methadone or sublingual buprenorphine as pharmacotherapy for the treatment of opioid dependence	• Children and young people aged 17 years or younger
Interventions of interest	
• Models of care that include the provision of methadone or sublingual buprenorphine as pharmacotherapy for the treatment of for opioid dependence in unsupervised settings	• Models of care involving only the supervised provision of methadone or sublingual buprenorphine as pharmacotherapy for opioid dependence
Language	
• English	• Languages other than English
Country	
• High-income countries according to the World Bank classification system (New Zealand, Canada, UK, US, Nordic countries (e.g. Norway, Sweden)	• Countries other than those listed

Inclusion criteria	Exclusion criteria
Year of publication	
• 2020 onwards [note: 100 citations from a Google Scholar search organised by relevance were harvested and screened. Therefore, some included studies were published before 2020]	• 2019 and earlier

Data extraction

Eligible studies were divided into two categories representing the different evidence types considered: 1) systematic reviews, and 2) primary studies. Categorising studies in this way also helped to avoid duplication by ensuring that data from primary studies included within systematic reviews were not extracted twice. Data were then extracted separately for each category using the eligibility criteria summarised in **Table 2** below.

Table 2: Eligibility criteria for identified studies

Systematic reviews
Author, date, aims, number of quality criteria met / total applicable criteria
Number of studies included in the review
Primary intervention focus
Overall review findings (including risks / adverse events)
Key conclusions reported by study authors (headline findings, headline conclusions about the strength of evidence contained in the review)
Primary studies
Author, year, country, number of quality criteria met / total applicable criteria
Study aim
Study design, setting, location, COVID-19 context (i.e. study conducted in the context of COVID-19 restrictions or not)
Sample size
Intervention: primary intervention of interest as reported by the study authors, including treatment characteristics: • Supervised versus unsupervised (e.g. COVID-19 natural experiment) • Methadone versus SL buprenorphine • Frequency of clinical contact

- Service type (primary care; specialist care; therapeutic alliance; adjunctive treatment (e.g. counselling); integrated care for co-occurring conditions; overdose prevention; use of peer workers)
- Setting (general practice; specialist; clinic; pharmacy)
- Clinician type and experience level
- Location (metro; rural; remote)
- Country and any country-specific service characteristics that may impact generalisability of intervention/treatment to NSW

Control (and other secondary interventions, where there is a control group)

Outcomes, including (but not limited to):

- Safety: patient and community related poisoning; overdose and related mortality; diversion / misuse
- Effectiveness: treatment retention; illicit substance use; patient satisfaction / experience; quality of life (QoL)

Key conclusions reported by study authors

Quality appraisal

The methodological quality of systematic and narrative reviews was evaluated using the AMSTAR 2 tool[12] and SANRA[13] tools, respectively. The methodological quality of included primary studies was evaluated at two levels:

1. Strength of study design, ranked according to the NHMRC Hierarchy of Evidence[14]
2. Quality of study methodology using an appropriate tool for study design (relevant JBI critical appraisal tool or National Institutes of Health (NIH) quality assessment tool).

Table 3 outlines the NHMRC Hierarchy and associated quality appraisal tools. **Appendix 3** presents the results of all quality appraisal for all included studies.

Based on the high review yield, we undertook dual independent quality appraisal for 10% of studies, with all other studies undergoing a single quality appraisal.

We used a number of different quality appraisal tools. Certain quality appraisal criteria were not relevant for some studies. We therefore evaluated study quality according to the proportion of applicable quality criteria met, where:

- High quality was defined as meeting > 75% of applicable criteria
- Medium quality was defined as meeting 50% – 75% of applicable criteria
- Low quality was defined as meeting < 50% of applicable criteria.

Table 3: Classification of study designs and critical appraisal tools

	Study design and definition	Indicative appraisal tool
I	**A systematic review of level II studies** *"Systematic location, appraisal and synthesis of evidence from scientific studies."* (Coleman et al. 2008) Note: The NHMRC definition specifies that systematic reviews focus on Level II studies (randomised controlled trials). Reviews in this topic area may not contain or be exclusive to RCTs. Study designs of included studies in reviews will be noted in the review findings. **(Narrative, scoping and rapid reviews will also be included)**	AMSTAR 2 (systematic reviews); SANRA narrative reviews)[12,13]
II	**A randomised controlled trial** *"Experimental studies meet three conditions: manipulation, control and random assignment. Specifically, the researchers manipulate the intervention of interest and the control condition and they randomly allocate the participants to the intervention or control group. Random allocation refers to an authentically random process such as the toss of a coin or use of a table of random numbers" (p. 72) (Shadish W, Cook TD, Campbell DT, 2002)[78].*	The revised JBI critical appraisal tool for the assessment of risk of bias for randomised controlled trials[15]
III-1	**A pseudo-randomised controlled trial (i.e. alternate allocation or some other method)** *" … allocation may not use an authentically random process. For example, if investigators use alternate group allocation like even and odd dates, they cannot ensure that each participant has an equal chance of landing in either group. Experimental studies without authentic random allocation but using systematic alternate group allocation methods mentioned above are experimental studies with pseudo randomisation, or pseudo-RCTs" (p. 72) (Shadish W, Cook TD, Campbell DT, 2002)[78].*	JBI checklist for quasi-experimental studies (non-randomised experimental studies)[16]
III-2	**A comparative study with concurrent controls**	JBI checklist for quasi-experimental studies (non-randomised experimental studies)[16]
	Non-randomised experimental trial: "*Quasi-experimental studies are studies where the intervention of interest and the control condition are controlled (manipulated) by the researchers, however, the allocation of participants is not a random, systematic or pseudo-random allocation. Frequently, participants self-select into groups or the researchers decide which persons should get the intervention and which persons should get the control" (Shadish et al, 2002)[78].*	JBI checklist for quasi-experimental studies (non-randomised experimental studies)[16]
	Cohort study: *"… outcomes for groups of people observed to be exposed to an intervention, or the factor under study, are compared to outcomes for groups of people not exposed".* Prospective = followed prospectively with further outcomes recorded as they happen; retrospective = defined at a point of time in the past and information collected about subsequent outcomes (NHMRC 2009)[79].	JBI checklist for cohort studies[17]

	Study design and definition	Indicative appraisal tool
	Case-control study: *"… people with the outcome or disease (cases) and an appropriate group of controls without the outcome or disease (controls) are selected and information obtained about their previous exposure/non-exposure to the intervention or factor under study"* (NHMRC 2009)[79].	JBI checklist for case control studies[18]
	Interrupted time series with a control group: *"… trends in an outcome or disease are measured over multiple time points before and after the intervention (factor under study) is introduced to a group of people, and then compared to the outcomes at the same time points for a group of people that do not receive the intervention (factor under study)"* (NHMRC 2009)[79].	JBI checklist for case control studies[18]
III-3	**A comparative study without concurrent controls**	
	Historical control study: *"… outcomes for a prospectively collected group of people exposed to the intervention (factor under study) are compared with either (1) the outcomes of people treated at the same institution prior to the introduction of the intervention (i.e. control group/usual care), or (2) the outcomes of a previously published series of people undergoing the alternate or control intervention"* (NHMRC 2009)[79].	JBI checklist for case control studies[18]
	Two or more single arm studies: *"… the outcomes of a single series of people receiving an intervention (case series) from two or more studies are compared"* (NHMRC 2009)[79]	JBI checklist for case series[19]
	Interrupted time series without a parallel control group: *"… trends in an outcome or disease are measured over multiple time points before and after the intervention (factor under study) is introduced to a group of people, and compared"* (NHMRC 2009)[79]	JBI checklist for quasi-experimental studies (non-randomised experimental studies)[16]
IV	**Case series** with either post-test or pre-test / post-test outcomes.	The National Institutes of Health (NIH) quality assessment tool for before-after (pre-post) study with no control group[20], OR JBI checklist for case series[19]
	Cross-sectional study*: "… a group of people are assessed at a particular point (or cross-section) in time and the data collected on outcomes relate to that point in time"* (NHMRC 2009)[79]	JBI checklist for analytical cross-sectional studies[21]

Data analysis and reporting

Given that the interventions, populations targeted, and outcomes measured, varied substantially across studies, a meta-analysis was not appropriate. Therefore, we undertook a narrative synthesis of findings, including commentary about the implications of the Evidence

Check findings in the context of NSW / Australian policy and practice. Findings from systematic reviews were summarised separately to the findings of primary studies. As the pandemic significantly influenced service delivery models, provision of unsupervised dosing, drug markets and access to opioid dependence treatment, studies that were identified as being studies of COVID-19 policy changes, and those which noted that they were conducted during the pandemic were considered separately.

Methods: Question 2

To inform the NSW *Guidelines for the Treatment of Opioid Dependence*, it is important to situate these within the broader national and international context to understand best practice in medication choice, dosing and models of care. This is particularly relevant given recent developments in opioid dependence treatments, including the availability of long-acting injectable buprenorphine, and the evolving evidence base for the use of alternative opioids such as slow-release morphine. By comparing publicly available guidelines and related grey literature across jurisdictions with comparable health systems and socioeconomic contexts, this desktop review sought to highlight consistencies and divergences in clinical recommendations and identify areas where there is potential for innovation in local practice.

Search strategy

An online desktop review was conducted to identify grey literature published from 2020 to August 2025, and that was comparable in scope and intent to the *NSW Guidelines for the Treatment of Opioid Dependence*. The review targeted publicly available policy documents, reports and clinical guidelines related to best practice pharmacological management of opioid dependence.

The search covered:

1. **Other Australian states and territories**, to capture variation within national practice, focusing on guidelines published since 2020.
2. **At least two international comparators** with health systems and socioeconomic characteristics similar to Australia (e.g. Canada, the UK, Norway, the US).

The websites of key health and regulatory agencies (such as health departments, public health agencies and peak bodies) were searched, and documents included if they:

- Provided clinical guidance or policy direction on opioid dependence treatment
- Were published in 2020 or later
- Reported outcomes for one or more of the following medications: methadone, sublingual buprenorphine, long-acting injectable buprenorphine, slow-release morphine, or other opioids used in treatment (e.g. hydromorphone).

Data extraction

A coding matrix was developed a priori to ensure consistency of data extraction across Australian jurisdictions. For each eligible document, information related to the variables of interest summarised in **Table 4** was extracted where available.

Table 4: Key variables of interest

Key variables of interest
Medication type
Clinical setting (e.g. community pharmacy, clinic, general practice)
Patient characteristics (e.g. age, comorbidities, eligibility criteria)
Dosing parameters (initiation, maintenance and maximum doses)
Takeaway dosing rules and supervision requirements
Supportive treatment requirements (e.g. psychosocial support, counselling)
Other prescriber / patient limitations
Frequency of patient access.

For international jurisdictions, the following contextual information was also extracted where available:

- Patterns of drug use and harms (e.g. prevalence, primary drugs of concern, morbidity and mortality)
- Underlying treatment philosophy (e.g. harm reduction, recovery-oriented approaches)
- Health system characteristics relevant to opioid dependence treatment.

Extraction was undertaken by the lead researcher (SN) using the coding matrix in Excel.

Data analysis and reporting

Extracted data were tabulated to allow comparison within and between jurisdictions. The synthesis highlights similarities and differences in clinical recommendations, dosing limits, supervision practices and underpinning philosophies of care.

For international jurisdictions, contextual factors such as treatment philosophy, health system structure, and patterns of drug use were considered to interpret clinical guidance within the broader context and healthcare environment.

The synthesis aimed to identify areas where current practice was already consistent with international best practice, as well as innovative approaches that could inform future updates to the NSW Guidelines. Findings were summarised narratively and supported by tabulated data.

Results: Question 1

Search results

Following searching and deduplication, 2462 titles and abstracts and 110 full-text studies were screened independently by two researchers. A total of 38 studies met inclusion criteria (see PRISMA diagram in **Appendix 2** for further detail). The included studies comprised:

- 6 systematic reviews (**Appendix 4**):
    - 2 systematic reviews: **pre-COVID**[8,22]
    - 4 systematic reviews: **during-COVID**[6,23–25]
- 32 primary studies:
    - 6 studies of contingent versus noncontingent take-home doses (**Appendix 5**, Table 1)[26–31]
    - 6 studies of unsupervised treatment (**Appendix 5**, Table 2)[32–37]
    - 4 studies of unsupervised buprenorphine induction (**Appendix 5**, Table 3)[38–41]
    - 9 primary studies conducted during the COVID-19 pandemic (**Appendix 5**, Table 4)[7,42–49]
    - 6 studies of remote supervision (**Appendix 5**, Table 5)[50–55]
    - 1 study not classified in the above categories.[56]

We identified an additional three ongoing studies of interest which we have included in **Appendix 6**, Table 1.

Overall, there is limited evidence to suggest supervision of buprenorphine dosing improves patient outcomes. Few studies identified in the Evidence Check assessed community safety from unsupervised buprenorphine dosing (see executive summary table for overview), though multiple population level studies in Australia, the UK and France suggest buprenorphine contributes to relatively less overdose mortality, even when diverted to people who are not in treatment.[57–59]

There are fewer studies of unsupervised methadone, though studies with methadone takeaways provided in a contingency management framework (i.e. where provision of takeaway doses is contingent on meeting a behavioural goal such as regular attendance or providing drug-free urine samples) suggest providing takeaway doses linked to patient outcomes can improve treatment outcomes. The number of methadone takeaway doses examined typically was limited (e.g. two per week); however at least one study examined weekly methadone provision (Gerra et al. 2011)[27]. Studies conducted in the context of the COVID-19 pandemic showed that even with large increases in unsupervised methadone dosing (14 and 28-day supplies provided), there was little evidence to suggest there was an impact on patient or community safety. Some studies suggest the level of supervision with methadone is important,

though evidence that could support a strong recommendation about the number of takeaway doses to offer at any point in treatment was not identified in the Evidence Check.

Evidence from Systematic reviews conducted pre-COVID (n=2)

Key messages:

- A review of unsupervised buprenorphine induction supported that it was a feasible alternative to supervised induction (noting that in the US context, most ongoing buprenorphine treatment is already completely unsupervised)
- A Cochrane review found overall there was limited evidence of safety concerns or poorer treatment outcomes, though most primary studies were judged to be of low to very low quality, and quality-of-life outcomes were rarely examined. When considering application to the NSW context, it is important to note that many studies were older, conducted largely with methadone, and that the conditions of takeaway provisions varied; details of this level were considered in reviews of primary studies.

Two systematic reviews from 2014 and 2017 examined different aspects of unsupervised or TA dosing.

A Cochrane review by Saulle et al. (2017)[8] specifically comparing supervised dosing with 'off-site consumption' (n = 6 studies, 7999 people receiving methadone [7786 people] or buprenorphine–naloxone [213 people]), and found providing TA doses had no effect on retention, abstinence, diversion or mortality, noting most evidence was deemed to be low to very low quality. The one included study that measured diversion reported 5% in the supervised group compared with 2% in the unsupervised group, with the apparent higher rate of diversion in the supervised group not determined to be statistically significant, and was judged as low-certainty evidence.

A second review published by Lee et al. (2014)[22] **examined 10 studies of unsupervised buprenorphine induction**, concluding that, compared with observed buprenorphine induction, unsupervised induction did not seem to be associated with disproportionate adverse events or lower treatment retention rates.

Both systematic reviews had AMSTAR 2 scores of 8/13 (moderate quality) and 16/16 (high quality), respectively. Of note, the Cochrane review was considered to present high-quality evidence, though the review itself concluded that "at present, there is uncertainty about the effects of supervised dosing compared with unsupervised medication due to the low and very low quality of the evidence" in the individual studies examined. The AMSTAR scoring system for systematic reviews does not recommend a range considered 'high' or 'low' quality; instead, it recommends considering which applicable criteria were or were not met. Both studies met

AMSTAR's threshold of > 50% criteria and therefore were considered to be of a relatively high quality.

Outcomes: Safety and effectiveness

Safety

Patient and community related poisoning / overdose, and related mortality

Lee et al. (2014)[22] concluded unsupervised buprenorphine induction did not seem to be associated with disproportionate adverse events. Saulle et al. (2017)[8] did not find supervision influenced mortality outcomes. Notably, both these reviews assessed only patient safety, not community safety.

Diversion / misuse

Not reported.

Effectiveness

Treatment retention

Saulle et al. (2017)[8] and Lee et al. (2014)[22] both found providing unsupervised doses did not change retention.

Illicit substance use

Saulle et al. (2017)[8] found providing takeaway doses was not associated with differences in substance use outcomes.

Patient satisfaction / experience

Not reported.

Quality of life

Not reported.

Evidence from systematic reviews conducted during COVID (n=4)

Key message:

Evidence from four systematic reviews conducted during the COVID-19 pandemic indicates that provision or expansion of methadone takeaway treatment did not appear to be associated with negative outcomes (e.g. no increased risks of overdose, mortality or diversion), while improving patient experience and reducing treatment burden.

Four reviews examined the impact of increased opioid dependence treatment takeaway dosing in the context of the COVID-19 pandemic.

A systematic review of relatively higher quality by Adams et al. (2023)[6], drawing on 40 studies from Canada, the US, the UK, Australia, Bangladesh and Malaysia, found relaxing takeaway dose restrictions improved patient experiences and reduced treatment burden, with no evidence of increased substance use or overdose.

Brown et al. (2024)[23] , in a review of adaptations to service provision reported by nursing professionals, similarly observed an expansion of TA provision but reported no clear signs of diversion or nonmedical use.

Krawczyk et al. (2023)[24] synthesised qualitative evidence from US studies relating to the public health emergency orders allowing for increased TAs, noting that while some providers worried about concurrent use of other drugs (e.g. sedatives), many patients described increased TA doses as enhancing self-esteem, autonomy and treatment engagement. Some patients felt excluded from these flexibilities, with the lack of TA doses seen as burdensome and a disincentive to engagement. In this review, diversion was also reported to be rare and no increase in methadone overdoses was detected.

Naher et al. (2024)[25] conducted a systematic review of studies in Canada during the COVID-19 period, identifying greater provision of TA, but outcomes such as overdose were not reported, and data relating to the key themes was limited, mentioning primary study of remote supervision.

Study quality

There were four systematic reviews of which two (Adams et al. 2023[6], Naher et al. 2024[25]) were high quality (AMSTAR 2 11/13 and 10/13 respectively) with AMSTAR 2 scores ranging from 5/13 (low quality) to 11/13 (high quality). Two of the reviews were low quality (Brown et al. 2024[23] and Krawczyk et al. 2023[24]).

Outcomes: Safety and effectiveness

Safety

Patient and community related poisoning / overdose, and related mortality

Krawczyk et al. (2023)[24] found providing TA doses did not change mortality before or during the pandemic. Adams et al (2023)[6] found no evidence that offering take-home doses to previously ineligible clients changed rates of overdose.

Diversion / misuse

Krawczyk et al. (2023)[24] found diversion to be rare, and similarly Brown et al. (2024) observed no clear signs of diversion or nonmedical use associated with increased TA provision.

Effectiveness

Treatment retention

Not reported.

Illicit substance use

Adams et al. (2023)[6] found no evidence that offering take-home doses to previously ineligible clients changed rates of substance use. Krawczyk et al. (2023)[24] found some providers expressed concern that patients continued to use substances such as sedatives.

Patient satisfaction / experience

Adams et al. (2023)[6] found take-home doses reduced clients' exposure to unregulated substances and stigma and minimised work / treatment conflicts. Consistent with this, Krawczyk et al. (2023)[24] reported many patients described increased TA doses as enhancing self-esteem, autonomy and treatment engagement. Some patients felt excluded from these flexibilities, with the lack of TA doses seen as burdensome and a disincentive to engagement.

Quality of life

Not reported.

Evidence from primary studies of contingent takeaway doses (n=6)

Key messages:

- Linking provision of takeaway doses to treatment attendance, stability or engagement supports better retention and lower substance use
- Routine noncontingent provision of takeaway does (not linked to these outcomes) does not appear to offer the same benefits
- Routine provision of takeaways not linked to attendance or stability may increase risks for the person in treatment as well as the community because of increased diversion and greater substance use
- More specifically, when provision of seven takeaway doses of methadone was linked to stability and drug-free urines better outcomes were seen compared with providing the same number of takeaway doses that were not contingent on outcomes
- Similarly, when up to 28 days of buprenorphine was provided linked to monitoring of adherence, this was associated with less substance use
- Older studies of contingent methadone doses tended to only provide single doses for short periods of time, which, while linked with improved outcomes such as attendance, may be less applicable to long-term methadone treatment in NSW where attending counselling multiple times per week is uncommon.

Six studies examined the use of takeaway methadone doses within a contingency management framework. Most were conducted some time ago in diverse countries, including Italy, Israel, the United Arab Emirates and the US. In these studies, takeaway doses were used as rewards for desired behaviours, such as attending counselling or providing drug-free urine samples, to reinforce positive treatment outcomes.

Individual studies are described below, with results then synthesised by safety and effectiveness outcomes following the individual study descriptions.

Gerra et al. (2011)[27] conducted an observational study across three services in Italy with different methadone-dosing policies: a) supervised daily consumption with one takeaway on Sundays, b) contingent supervised doses (provided with seven-day takeaway doses for stability, program adherence and drug-free urines), and c) one supervised dose with weekly takeaway doses provided from treatment commencement (i.e. takeaway doses not based on stability or substance use outcomes). Participants appeared comparable on baseline measures,

though sites were not randomised. Those with takeaway doses based on stability and drug-free urines had higher retention than the other two groups, but there was no difference in substance use between those with conditional takeaways and those who had supervised dosing. Those with noncontingent takeaway doses had higher rates of crime, diversion and positive urines, and no better retention compared with supervised treatment.

Elarabi et al. (2021)[26] conducted a randomised controlled trial (RCT) of incentivised unsupervised dosing in the UAE where both groups received buprenorphine maintenance with stepped access to take-home doses. The intervention group had additional monitoring (UDS plus blood concentration checks) with the possibility of progressively larger take-home supplies (up to 28 days), whereas the control group was limited to a maximum of 14 days of takeaway doses with no blood-level monitoring. This study found more urine monitoring with contingent takeaway doses led to lower opioid use, but did not affect retention.

Kidorf et al. (1994)[28] conducted two (n = 10, n = 15) within-patient randomised studies demonstrating contingent reinforcement of therapy attendance with methadone takeaway doses. The reinforcement effect was strongest when each therapy session was incentivised by a methadone take-home dose.

Peles et al. (2011)[29] conducted an observational study (n = 657) in Israel that found patients who earned contingent unsupervised methadone takeaway doses sooner were likely to have better long-term treatment outcomes in terms of retention and substance use, though the observational nature of the study means it is not possible to rule out confounding, with those patients who were receiving takeaway doses likely to be the patients that were able to meet the conditions required (i.e. those receiving takeaway doses were able to reduce their substance use, and those who were not able to do this in order to receive contingent takeaway doses had a poorer overall prognosis).

Stitzer et al. (1992)[31] conducted a US study (n = 53) of contingent unsupervised take-home methadone doses (up to three non-consecutive takeaway doses a week). Providing takeaway doses on a contingent basis after two or more consecutive weeks of drug-free urines was more effective in promoting drug-free urine submissions than take-home medications provided on a noncontingent, or random delivery schedule. No effect was observed on treatment retention.

Stitzer et al. (1977)[30] also conducted an earlier US study with alternating noncontingent, and contingent methadone takeaway doses provided based on participation in weekly counselling sessions (n = 16). Participation was found to be significantly higher during the contingent periods compared with noncontingent periods, demonstrating that weekend medication takeaway doses can serve as an effective reinforcer for attendance in methadone treatment.

Study quality

In this section there was one randomised controlled trial, three within patient-randomised or quasi-randomised trials, and two observational studies, with quality assessments indicating each study met the majority of quality criteria in the quality appraisal and two studies receiving the maximum possible study quality score. Based on the study designs and quality, moderate confidence can be placed in study findings. This should be borne in mind when interpreting and applying review results.

The majority of these studies were conducted at least 15 years ago, with only one study that examined contingent provision of methadone doses in the past five years. However, there is a broad and ongoing body of literature supporting that contingent reinforcement remains an evidence-based strategy for a range of substance use disorders, suggesting the findings are likely to have ongoing relevance.

Outcomes: Safety and effectiveness

Safety

Patient and community related poisoning / overdose, and related mortality

No study directly reported on the outcomes of patient of community safety as they relate to poisoning or mortality.

The study of three treatment centres in Italy that tested three different conditions of takeaway dose provision found those receiving noncontingent unsupervised dosing were 3.5 times more likely to commit crimes / violence than those who received supervised methadone and those where methadone takeaway doses were provided conditional on providing drug-free urine tests, being on a stable methadone dose, having housing and adherence to the other program rules, which may indirectly affect community safety (Gerra et al. 2011)[27].

Diversion / misuse

In the same Italian study, diversion was higher with noncontingent takeaway methadone dosing than when takeaway dosing was dependent on demonstrating stability and meeting behavioural conditions (Gerra et al. 2011)[27].

Effectiveness

Across diverse settings, studies consistently showed contingent access to methadone and buprenorphine takeaway doses was associated with improved treatment effectiveness outcomes as detailed below.

Treatment retention

Retention was higher when takeaway doses were contingent on stability in studies of methadone treatment in Italy and Israel and buprenorphine treatment in the UAE (Gerra et al. 2011[27]; Peles et al. 2011[29], Elarabi et al. 2021[26]).

Counselling attendance and engagement also increased in earlier studies in the US when each session was reinforced by the opportunity to earn a methadone takeaway dose (Kidorf et al. 1994[28]; Stitzer et al. 1977[30]).

Illicit substance use

Substance use outcomes improved when takeaway doses of methadone and buprenorphine were conditional on providing drug-free urines or additional monitoring, with one US study finding the drug-free urines increased with takeaway doses conditional on meeting requirements and decreased with noncontingent takeaway doses (Elarabi et al. 2021[26]; Stitzer et al. 1992[31]). For example, the study in the United Arab Emirates found 77% of urines were opioid-free in the contingent takeaway condition compared with 64% in the standard-care condition.

In the Italian study, noncontingent take-home methadone dosing was associated with *greater* substance use, but there were no differences in substance use between those with takeaway doses conditional on demonstrating stability and providing drug-free urines and those who received supervised dosing with a single takeaway dose per week (Gerra et al. 2011[27]).

The Kidorf et al. (1994)[28] US study found provision of methadone takeaway doses conditional on counselling attendance did not lead to reduced drug use, despite increasing counselling attendance, though the authors attributed this to the short time period of the contingent dosing (three-to-six weeks).

Patient satisfaction / experience

Not reported.

Quality of life

Not reported.

Evidence from primary studies of unsupervised treatment (n=6)

Key messages:

- Unsupervised treatment with buprenorphine can achieve equivalent outcomes to supervised dosing
- Unsupervised buprenorphine treatment was clearly superior to no treatment
- Outcomes with unsupervised treatment with methadone appear more sensitive to the degree of supervision and patient stability
- For both medications, diversion and associated risks remain an important consideration.

Six studies examined outcomes associated with unsupervised dosing (i.e. treatment where no doses are supervised in a pharmacy or clinic). Four studies examined unsupervised dosing of buprenorphine-naloxone: two were conducted in Australia (Dunlop et al. 2017[32]; Bell et al. 2007[33]) and two were conducted in the US (Sigmon et al. 2023[34], Binger et al. 2020[36]). Two studies examined unsupervised methadone dosing, in the UK (Haskew et al. 2008[37]) and Ireland (Cousins et al. 2017[35]). It should be noted that across the countries and time periods covered by these studies, there were substantial differences in policies governing unsupervised dosing, particularly between methadone and buprenorphine with respect to the number of take-home doses permitted, and time in treatment required for eligibility, or whether supervised dosing was a requirement at any point in treatment. This differs from the NSW context where supervised dosing in a pharmacy or clinic is a routine part of care for both treatments, notably in the first three months of treatment.

Dunlop et al. (2017)[32] conducted an RCT that compared unsupervised buprenorphine-naloxone dispensed weekly (after an in-clinic induction) with a waitlist control group (i.e. untreated) (n = 50) in Australia, finding unsupervised buprenorphine treatment resulted in 19 days less heroin use per month, in addition to lower scores for crime and higher scores for quality of life and mental health outcomes.

Bell et al. (2007)[33] conducted an RCT comparing weekly unsupervised versus supervised dosing with buprenorphine-naloxone in Australia (n = 119). Retention and heroin use was not significantly different between observed and unobserved dosing groups. No difference was observed in quality of life. One adverse event involving injection of buprenorphine-naloxone was reported in the unsupervised group. There were 18 reports of diversion of trial medication (i.e. diversion of unsupervised doses) during the study.

Sigmon et al. (2023)[34] conducted two randomised controlled trials in the US (n = 50 per trial) **comparing unsupervised buprenorphine** (after an in-clinic induction, and provision of a device with timed windows for medication access) **with provision of harm reduction information** (and no treatment) **in non-rural** (Trial 1) **and rural** (Trial 2) **settings**. In both trials, patients randomised to receive unsupervised buprenorphine treatment were significantly more likely to be abstinent from illicit opioids, with very high treatment adherence.

Cousins et al. (2017)[35] examined the association between supervised methadone dosing and retention in an observational cohort of patients over multiple treatment episodes (n = 6393). They found a j-shaped response curve, where regular supervision (20% – 60% of doses) was associated with better retention relative to minimal supervision (< 20% of doses), but greatest risk of treatment cessation was associated with higher frequency supervision (> 60% of doses). Median daily doses between 60 mg and 120 mg and multiple treatment episodes were also associated with greater retention. Given this is an observational study where patients were not randomised to supervision conditions, results may in part reflect that less stable patients received more supervised dosing as part of clinical policy.

Binger et al. (2020)[36] published a US retrospective cohort study of people in buprenorphine-naloxone treatment that compared relapse rates between patients with daily dosing versus unsupervised doses. The study was primarily designed to examine the impact of buprenorphine-naloxone dose (high or low) on treatment outcomes. The study found

no effect of supervision on treatment outcomes, with higher dose (> 16 mg) being the primary driver of increased retention and reduced substance use. Safety outcomes were not reported by supervision status.

Haskew et al. (2008)[37] conducted interviews with patients collecting methadone from community pharmacies in the UK (n = 91). Dispensing of methadone without supervised dosing is more common in the UK than in NSW (i.e. not all patients are required to have doses under the direct supervision of a pharmacist, and guidelines recommend supervision primarily in the first three months of treatment). In this study, 40% of participants received at least some doses supervised in the community pharmacy (though the number of doses is not specified in the paper) while 60% had completely unsupervised methadone dosing. Thirty-eight participants (42%) were identified to be 'partial or poor adherers', and these patients were more likely to be prescribed completely unsupervised methadone. This group picked up fewer doses, though they were also less likely to have used heroin in the past month. Those with unsupervised doses were more likely to have sold, exchanged or given away doses, though the authors noted that supervised consumption did not ensure treatment adherence.

Study quality

Three papers were randomised controlled trials (Dunlop et al. 2017[32], Bell et al. 2007[33]; Sigmon et al. 2023[34]), two were observational studies with likely confounding by indication (Cousins et al. 2017[35]; Binger et al. 2020[36]), and one study was based on self-report survey data (Haskew et al. 2008[37]), representing the weakest evidence. Quality assessments indicated most studies met at least half the quality appraisal criteria. Based on the study designs and quality appraisal findings, moderate confidence can be placed in study findings. This should be borne in mind when interpreting and applying review results.

Outcomes: Safety and effectiveness

Safety

Patient and community related poisoning / overdose, and related mortality

Dunlop et al. (2017)[32] found no deaths in either group were reported during the study period or 12 months after study completion, assessed by confirmation with the National Coroners Information System.

Diversion / misuse

Some reports of diversion and injection misuse were reported with unsupervised buprenorphine (Bell et al. 2007[33]) and with unsupervised methadone (Haskew et al. 2008[37]). Use of a device with timed windows for medication access intended to reduce diversion of buprenorphine was associated with very high rates of treatment adherence (99% of doses were taken as scheduled; Sigmon et al. 2023[34]). A lack of supervised methadone consumption was related to partial or poor adherence; however, diversion also occurred among participants who had

supervised dosing (e.g. 14% of the whole sample admitted to giving away doses of methadone in the past month; Haskew et al. 2008[37]).

Effectiveness

Treatment retention

When unsupervised buprenorphine treatment was compared directly with supervised dosing, retention was generally similar (Bell et al. 2007[33]; Binger et al. 2020[36]). Provision of a higher dose was a larger influence on clinical outcomes (e.g. rate of relapse was lowered and time to relapse was lengthened with doses > 16 mg) (Binger et al. 2020[36]). Methadone retention followed a j-shaped curve, with better outcomes when some supervision was provided (20% – 60% of doses supervised), but poorer retention when most doses (> 60%) were supervised (Cousins et al. 2017[35]), although this most likely reflects patients who were higher risk or had more complex profiles receiving higher levels of supervision.

Illicit substance use

When compared with no treatment, unsupervised buprenorphine was associated with significant reductions in heroin use (Dunlop et al. 2017[32]) and higher rates of abstinence from illicit opioids (Sigmon et al. 2023[34]). When compared directly with supervised dosing, substance use outcomes were generally similar (Binger et al. 2020[33]).

In the survey study by Haskew et al. (2008)[37], supervision arrangements were associated with distinct patterns of methadone and heroin use. Some patients (14%) had consumed only a portion of their dose on their last day of illicit heroin use, all of whom were receiving unsupervised methadone. Most patients who had missed their full dose of methadone on the last day they used heroin were receiving supervised methadone doses. This suggests patients may miss doses altogether if doses are supervised, whereas they may titrate dosing rather than miss doses completely when they are able to through unsupervised dosing conditions.

Patient satisfaction / experience

Overall satisfaction with unsupervised buprenorphine treatment was high among patients in both rural and non-rural areas (mean rating of 4.9/5), with slightly lower satisfaction ratings for the portable device intended to reduce diversion (mean ratings of 3.9–4.1/5) (Sigmon et al. 2023[34]).

Quality of life

Compared with no treatment, unsupervised buprenorphine was associated with improvements in mental health and quality of life (Dunlop et al. 2017[32]; Sigmon et al. 2023[34]).

Evidence from primary studies on unsupervised buprenorphine induction (n=4)

Key messages:

- Four smaller studies found unsupervised buprenorphine induction appears feasible and can offer benefits of increasing flexibility without compromising safety
- Retention rates for unsupervised buprenorphine induction appear comparable to observed induction (where a control arm was included in the study)
- Where supervised induction is not possible, unsupervised induction could offer a feasible alternative. Developing and testing protocols in the NSW context could support upscaling of these methods
- Findings from one study, while preliminary, suggest unsupervised induction from methadone may result in a higher rate of prolonged withdrawal symptoms, and prior buprenorphine exposure improved success. This could inform patient selection for unobserved induction
- Studies were conducted in the context where ongoing buprenorphine treatment does not typically involve supervised dosing, in contrast to the current NSW context where supervised dosing is usual at treatment commencement.

Four studies examined outcomes associated with unsupervised buprenorphine induction. All four studies were conducted in the US. Patients who received unsupervised buprenorphine induction self-administered their initial and subsequent doses of buprenorphine (i.e. without direct observation in a clinical setting) following provision of a prescription along with detailed instructions about dosage and timing to avoid precipitated withdrawal.

Individual studies are described below, with results then synthesised by safety and effectiveness outcomes following the individual study descriptions.

Green et al. (2023)[60] conducted a pilot RCT (n = 100) of physician-delegated unsupervised buprenorphine induction by pharmacists. Pharmacists were trained to implement unobserved induction and confirm the treatment regimen (overseen by a collaborating addiction medicine physician). Patients who stabilised (n = 58) were randomised to receive follow-up care in the pharmacy or with the provider (usual care). Retention was higher in the pharmacy follow-up care group.

Gunderson et al. (2010)[40] conducted a pilot RCT (n = 20) comparing observed versus unsupervised buprenorphine induction in a primary care setting. Safety and effectiveness measures included induction success, stabilisation, and complication rates. One unobserved induction patient experienced precipitated withdrawal but stabilised by week one. Milder

prolonged withdrawal occurred equally across both groups and stabilisation did not differ by induction method.

Krenz et al. (2022)[39] used retrospective data to examine outcomes for 35 patients with opioid dependence who had attended the emergency department (ED) and received a take-home supply of buprenorphine-naloxone. The presenting complaint at the ED was not reported, but was described to be commonly for treatment of an overdose, opioid withdrawal or opioid dependence. Thirty-five patients received their first dose of buprenorphine in the ED and 120 patients completed at-home induction. Outcomes were not reported according to whether induction was completely unsupervised or not. Overall, 45.2% of patients remained in buprenorphine treatment three months after unsupervised dosing following ED initiation, with this approach facilitating the induction of patients who were not yet in withdrawal (i.e. could not commence medication in the ED and hence might be lost to treatment if needing to return for dosing).

Lee et al. (2009)[38] published a case series (n = 103) demonstrating feasibility of home (unsupervised) buprenorphine induction with no safety concerns (i.e. no severe precipitated withdrawal or serious adverse events) reported or observed. Five patients reported mild-to-moderate withdrawal symptoms that were resolved by day three with additional buprenorphine dosing, while an additional five patients experienced prolonged unrelieved withdrawal symptoms, three of whom were inducted from methadone (3/14 or 21% of those who transitioned from methadone doses of 40 mg or below), highlighting that this may be a higher risk group for prolonged withdrawal. Those with prior buprenorphine exposure had higher odds of remaining in treatment.

Study quality

In this section there were two RCTs (Green et al. 2023[60] and Gunderson et al. 2010[40]), one retrospective cohort study (Krenz et al. 2022[39]) and one case series (Lee et al. 2009[38]). Quality appraisal scores varied from 8–9/13 for the RCTs to 7/11 for the case series. Based on the study designs and quality, moderate confidence can be placed in their findings. This should be borne in mind when interpreting and applying review results.

Outcomes: Safety and effectiveness

Safety

Patient and community related poisoning / overdose, and related mortality

No studies identified safety concerns associated with unsupervised induction. Of the patients who stabilised following pharmacist-led unsupervised induction (n = 58), three reported non-fatal overdoses (one in the pharmacy-based care group) and three reported non-opioid-related ED visits (two in the pharmacy-based care group) in the first month (Green et al. 2023[60]). It is notable that this study was conducted in the context of high overdose rates from synthetic opioids in the US. A second study (Krenz et al. 2022[39]) found 11% of patients returned to the ED with a non-fatal opioid overdose within six months, but did not report safety-related outcomes separately for observed versus unobserved induction.

Patient and community related poisoning / overdose, and related mortality

No studies identified safety concerns associated with unsupervised buprenorphine induction.

Green et al. 2023[60] reported that, of the patients who stabilised following pharmacist-led unsupervised induction (n = 58), three reported non-fatal overdoses (one in the pharmacy-based care group) and three reported non-opioid-related ED visits (two in the pharmacy-based care group) in the first month.

Krenz et al. 2022[39] reported that 11% of patients returned to the ED because of a non-fatal opioid overdose within six months. Safety-related outcomes were not reported separately for observed versus unobserved induction.

Both these studies were conducted in the context of a drug market with high levels of high-potency synthetic opioids, contributing to higher overdose rates in the community in general. This context, combined with the lack of a comparator, makes the frequency of overdoses difficult to interpret.

Diversion / misuse

Not reported.

Effectiveness

Treatment retention

Unsupervised induction was associated with outcomes comparable to supervised induction in regard to stabilisation and retention across a range of treatment settings including ED, primary care and pharmacy.

There were no significant differences in retention between patients who received buprenorphine in the ED compared with those who underwent home induction (Krenz et al. 2022[39]), measured by filling a buprenorphine prescription at three months (48.6% vs. 38.3%) or at six months (51.4% vs. 34.2%). In a study of pharmacy-initiated unobserved buprenorphine induction, 58/100 patients stabilised and went on to receive maintenance care (Green et al. 2023[60]). Pharmacy-based care was associated with significantly greater retention at one-month post-randomisation (89%) compared with usual care (requiring the participant to return to a clinic) 17%.

Compared with observed induction in a primary care setting, unsupervised induction had comparable outcomes in regard to successful induction (60%) and stabilisation (40%). Retention at four weeks was 50%, but was not reported separately for observed versus unobserved induction (Gunderson et al. 2010[40]). The case series of unsupervised buprenorphine induction (n = 103; Lee et al. 2009[38]) found retention was 59% at week 12 and 50% at week 24, with higher retention in those with prior buprenorphine exposure.

Illicit substance use

One study (Gunderson et al. 2010[40]) found 3/10 patients where data were available (i.e. who were retained at four weeks) used illicit opioids based on self-report or urine toxicology; this outcome was not reported separately for unobserved versus observed induction.

A case series of unsupervised buprenorphine induction (Lee et al. 2009[38]) found urine toxicology and self-report data indicated ongoing opioid use in a substantial proportion of patients, though there was no comparison arm. Among patients in treatment at 24 weeks, 24% had no positive urines for opiates or methadone throughout, 52% were intermittently positive, and 24% were positive throughout. Of note, self-reported opioid use declined from a mean of seven days a week at baseline to one day a week at week 12.

Patient satisfaction / experience

One study (Lee et al. 2009[38]) had unsupervised induction supported by a patient leaflet, which received positive feedback, while a telephone support line was relatively unused.

Quality of life

Not reported.

Other studies (n = 1)

One additional study was identified that did not fit into the above categories but contained data on a safety outcome, and is described below.

Safety

Medication errors

Gibson et al. 2020[56] examined medication error incidents related to pharmacotherapy for the treatment of opioid dependence, finding more incidents were related to supervised than to unsupervised dosing.

Evidence from primary studies of increased takeaway doses during the COVID-19 pandemic (n=9)

Key messages:

- Studies were largely observational or pre-post methods (representing weaker evidence), though some studies used population-level data and causal analysis methods that are considered to produce more robust findings
- Studies from the US, Canada, Australia and Europe consistently found expanded unsupervised (takeaway) dosing during COVID-19 and related policy changes did not worsen treatment or safety outcomes
- Expanded unsupervised dosing appeared safe, with some evidence for improved retention
- Monitoring for diversion remains important
- The context of these studies (during pandemic restrictions) may complicate interpretation.

US studies (Amram et al. 2021[42]; Panwala et al. 2023[48]; Hoffman et al. 2022[46]; Williams et al. 2023[49]; Barsky et al. 2025[43]) showed increased methadone takeaways were associated with stable or improved retention, reduced ED visits, with no clear increase in overdose.

Canadian (Gomes et al. 2022[45]), Australian (Lintzeris et al. 2022[7]) and Spanish (Narváez-Camargo et al. 2025[47]) data similarly reported no increased risk of overdose or treatment discontinuation, with some evidence of better retention among patients receiving additional takeaways.

A Canadian case series (Corace et al. 2022[44]) also found no rise in adverse events, though dose sharing was more common with more takeaway dose provision.

When considering the stable or reduced overdose rates and ED visits seen with increased takeaways in these findings, it is relevant to note that background rates of overdose were *increasing* in the US and Canada at this time because of the increased prevalence of potent synthetic opioids such as fentanyl in the illicit drug market.

Amram et al. (2021)[42] used a cross-sectional study design to evaluate the US Substance Abuse and Mental Health Services Administration (SAMHSA) exemptions that allowed increased unsupervised dosing at a clinic in Spokane (Washington state, US). This study (n = 183 patients on stable methadone doses) found a ‘near-doubling’ of take-home doses did not result in negative treatment outcomes, with reduced ED visits and no change in methadone adherence (measured with urinalysis) with increased unsupervised methadone dosing.

Panwala et al. (2023)[48] presented a second study using a pre-post design in the same region (Spokane, Washington, US), (n = 187) before and after increased methadone takeaway dose provision. Despite finding an increase in overall rates of urine drug screens detecting opioid use following the COVID−19 SAMHSA exemption, there was no association with increased takeaway doses and any significant change in rates of illicit opioid use.

Barsky et al. (2025)[43] conducted a retrospective cross-sectional study (n = 80,396) in Massachusetts (US), examining methadone, buprenorphine and naltrexone treatment initiation in patients released from incarceration. Methadone initiation rates (but not buprenorphine or naltrexone) increased after implementation of the expanded methadone takeaway policy, with no change in the non-fatal overdose rate and a higher fatal overdose rate before the increase in takeaways. The background rate of fatal overdoses increased in the same jurisdiction, making the findings of reduced overdoses notable, in addition to the increased treatment uptake.

Corace et al. (2022)[44] reported on a case-series (n = 402) examining increased unsupervised dosing of methadone, buprenorphine and slow-release oral morphine (SROM) during COVID, finding most patients (57%) had additional unsupervised doses, and those with additional doses were not more likely to report adverse events (overdose, ED or hospital admissions), though greater reporting of dose sharing and dose trading for food was reported among those with additional unsupervised doses.

Gomes et al. *(*2022)[45] conducted a retrospective propensity-weighted cohort study (n = 21,297) examining whether increased takeaway doses early in the COVID-19 pandemic in Canada was associated with treatment retention and opioid-related harm, finding no significant association between initiating takeaway doses and mortality, with those transitioning to takeaway doses of methadone having a lower risk of opioid overdose or treatment disruption or discontinuation than those with no change in take-home doses. The propensity weighting took into account age, sex, neighbourhood income quintile and urban location of residence, clinical profile (concurrent benzodiazepine prescription, alcohol use disorder, mental health diagnoses, chronic obstructive pulmonary disease, diabetes, HIV, pharmacotherapy dose, proportion of previous 28 days covered with pharmacotherapy) and health service use (recent opioid overdose, recent indication of stimulant-related harm or dependence, recent indication of sedative / hypnotic harm or dependence, number of opioid use disorder–related physician visits, number of non-opioid use disorder–related physician visits, ≥ 1 ED visits, ≥1 hospitalisations) (i.e. the two groups were made comparable by adjusting for differences in these variables). Findings were consistent among methadone recipients regardless of take-home dose level before the pandemic.

Hoffman et al. (2022)[46] conducted a mixed-methods analysis of urinalysis and electronic health record data combined with qualitative studies. The study examined increased provision of unsupervised methadone doses in 377 methadone patients in rural Oregon, finding no association with increased takeaways and substance use or retention among patients in treatment for at least 180 days who received more takeaways. In contrast, those in treatment for less than 90 days and did not receive additional takeaways were more likely to discontinue treatment in the post-COVID period.

Lintzeris et al. (2022)[7] used a pre-post design to compare outcomes (n = 429) before and after implementing policy changes involving unsupervised dosing in the context of COVID-19 in

NSW, Australia, finding no association between increased provision of unsupervised doses and increased substance use, with clinical deterioration more common in those with fewer unsupervised doses.

Narváez-Camargo et al. (2025)[47] conducted a retrospective observational study in 100 treatment centres in Spain (n = 10,609). Patients with longer dispensing intervals (collecting their doses every > 14 days) and hybrid care (in-person and telehealth) were significantly less likely to drop out of treatment, though the study did not present outcomes specifically by supervision levels.

Williams et al. (2023)[49] conducted a retrospective cohort study (n = 821) comparing patients initiating a new treatment episode of methadone maintenance in nine opioid treatment programs in the US during the COVID period compared with a historical control cohort. Most sites increased provision of methadone takeaways (a median increase of three days a month). Retention and risk of adverse events was comparable to a control group before the increased provision of takeaways during the COVID period, despite higher overall opioid use (excluding methadone) reported in the post-COVID period, though these results were not specifically linked to the number of takeaway doses provided to individual patients.

Study quality

All studies in this section were observational and likely to be confounded by the context. Most studies met the majority of quality appraisal criteria (scores varied from 7/11 to 11/11). When considering the study designs alongside the quality and context, low-to-moderate confidence can be placed in the findings. This should be borne in mind when interpreting and applying review results.

Outcomes: Safety and effectiveness

Safety

Patient and community related poisoning / overdose, and related mortality

Patient safety outcomes spanned a range of adverse effects such as overdose, ED presentations, all-cause deaths and opioid-related deaths. Across the studies there was stability (Corace et al. 2022[44]; Gomes et al. 2022[45]; Williams et al. 2023[49]), or even reductions (Amram et al. 2021[42]; Barsky et al. 2025[43]) in these adverse effects associated with COVID-related increases in takeaway doses.

Diversion / misuse

Not reported.

Effectiveness

Treatment adherence and retention

Barsky et al. (2025)[43] reported an increase in methadone initiation rates among people recently released from prison after the implementation of the expanded takeaway policy.

Three studies found treatment retention increased (Hoffman et al. 2022[46], Gomes et al. 2022[45] and Narváez-Camargo et al. 2025[47]) and in one it remained similar (Williams et al. 2023[49]) for the patients with COVID-related increased takeaway doses.

Illicit substance use

COVID-related increases in takeaway doses were associated with no changes or increased positive urine results. Hoffman et al. (2022)[46] found there were no significant changes in the proportion of positive urine drug results when patients in care for more than 180 days increased their methadone takeaway dosing from a median of eight to 13 a month. Similarly, Lintzeris et al. (2022)[7] did not find an association with increased substance use with increased methadone and buprenorphine-naloxone takeaways in NSW. In contrast, Williams et al. (2023)[49] did find an increase in non-methadone opioid use among the cohort of methadone patients starting treatment at the time of the increased takeaway policy in the US.

Patient satisfaction / experience

Patients reported improved satisfaction regarding the increases in takeaway dosing (Amram et al. 2021[42]) and improved patient–prescriber relationship including increased openness (Corace et al. 2022[44]). In qualitative interviews, patients valued the feeling of being trusted with increased responsibility, appreciated the reduced travel time, which increased employment and recreation, and reported reduced exposure to individuals who were less stable and potential triggers (Hoffman et al. 2022[46]).

Quality of life

Not reported.

Evidence from primary studies on remote supervision (n=6)

Key messages:

- Pilot studies into remote (e.g. video or smartphone) and/or electronic device (e.g. electronic pillbox) supervision of methadone and buprenorphine dosing suggest these approaches are generally feasible and acceptable, although the evidence base is preliminary
- Although adherence can be supported, evidence for broad appeal or improved clinical outcomes (e.g. reduced illicit opioid use) remains limited
- Tampering with devices was documented in studies that included higher-risk patients.

Video observation with a secure electronic pillbox

Janzow et al. (2022)[50] examined MySafeRx, a form of remote supervision of what would otherwise be unsupervised dosing of buprenorphine in a multisite RCT (n = 27). Remote supervision included daily videoconferencing with a mobile recovery coach, and a smartphone app that unlocked an electronic pill dispenser. Patient inclusion criteria included a past 30-day positive illicit drug screen or missed opioid toxicology screen with suspected illicit drug use as indicated by a clinical provider. The authors found the adherence monitoring platform was acceptable and feasible among those who entered the study, but the remote adherence monitoring did not appear to have broad appeal, with many declining to participate. No difference in illicit substance use as measured by urine drug screen was detected in the study.

Brooklyn et al. (2022)[52] examined video-observed dosing with a locked pillbox to support patients with travel hardship with methadone and buprenorphine medication adherence. The case series (n = 58) showed very low rates of nonadherence (< 0.1%) with remote supervision reducing treatment costs and travel time.

Video observation

Tsui et al. (2021)[51] conducted a pilot RCT that examined the feasibility of video-observed buprenorphine dosing compared with standard clinic-based treatment (weekly or bi-weekly visits with takeaway medicine) for patients initiating buprenorphine (n = 78). Video dosing was expected to improve adherence; however, no significant difference was found in clinical outcomes (i.e. reduction in illicit opioid use and greater engagement in treatment) between video-observed dosing and unsupervised dosing.

Hallgren et al. (2022)[53] examined video observation in a retrospective cohort study (n = 66) with program participants (n = 33) and matched controls (n = 33) showing program

participants had greater dose observation and were more likely to graduate to takeaway doses, concluding this was a feasible approach to supervised dosing and supported provision of more methadone takeaways.

Secure electronic pillbox

Kidorf et al. (2021)[54] conducted a prospective implementation study that examined an electronic pillbox in patients deemed to be more at risk from additional takeaways or more vulnerable to COVID-19 infections (n = 42). Results varied depending on the subgrouping used to support the rationale for the pillbox use: currently using illicit drugs or alcohol, vulnerable to take-home mismanagement, and acute medical problems or cognitive difficulties that impair tracking take-homes. Overall, some events of tampering were reported but the pillbox (which delivers up to 28 doses) appears a potential strategy to support unsupervised dosing in higher-risk individuals.

Sklar et al. (2024)[55] reported on a pilot study investigating an electronic pillbox, with a focus on feasibility (n = 24). Patients considered to have elevated risks for contracting COVID-19 infections were provided with 13 take-homes per visit and patients at risk of takeaway dose mismanagement were provided six methadone takeaways per visit. There was some evidence of tampering with the pillbox, though the authors considered it could still support safer takeaway dose provision.

Study quality

Two RCTs and four case series or pilot studies examined forms of remote dosing supervision. Quality appraisal scores varied from 5/9 or 7/13 to 9/10 though all were smaller studies. Low-to-moderate confidence can be placed in the study findings based on their designs and quality; it should be noted that most findings themselves were preliminary given the pilot nature of the studies.

Outcomes: Safety and effectiveness

Safety

Patient and community related poisoning / overdose, and related mortality

Hallgren et al. (2022)[53] and Kidorf (2021)[54] reported no participants experienced known overdoses during the study period. Janzow et al. (2022)[50] noted the daily monitoring resulted in clinical teams being better informed about daily patient activities.

Diversion / misuse

Studies commonly reported evidence suggestive of pillbox tampering. Kidorf (2021)[54] suspected 12 of the 42 study participants tampered with the pillbox, with repeated tampering messages leading to the removal of five patients from the pillbox study and returning to the standard

protocol. Similarly, Sklar (2024)[55] reported 54% of study participants possibly tampered with the pillbox. Janzow et al. (2022)[50] noted the videoconference plus electronic pillbox program informed clinical teams about the "pervasiveness of medication sharing". In contrast, the Brooklyn et al. (2022)[52] study received 98% of the monitoring videos expected and found only 0.1% of them showed signs of medication noncompliance.

Effectiveness

Treatment adherence and retention

Most studies with video monitoring components reported improved medication adherence: Janzow et al. (2022)[50]'s mobile recovery coaches confirmed supervised self-administration over videoconference for an average of 64% of applicable study days, Hallgren et al. (2022)[53] reported pilot participants uploaded a counsellor-accepted video 89% of the days in which the video was expected, and Brooklyn et al. (2022)[52] reported "medication ingestion integrity improved with the use of a secure medication dispenser". Brooklyn et al. (2022)[52] reported 98% of video patients were still in treatment 12 months later.

Within the context of common pillbox tampering and malfunctioning, the studies that provided electronic pillboxes but without daily video supervision still reported good adherence outcomes. Kidorf (2021)[54] reported that 99% of the scheduled take-homes were dispensed from the electronic pillboxes within the scheduled window of time and Sklar et al. (2024)[55] reported that 63% of pillbox patients missed at least one methadone dose, a mean of 0.76 doses per month.

Illicit substance use

Janzow et al. (2022)[50] reported no difference in intervention and control participants' urine drug screens for illicit substance use. Similarly, the Tsui et al. (2021)[51] RCT found that although 50% of the video-directly-observed patients returned negative urine samples compared with 64% of the treatment-as-usual participants, this was not a statistically significant difference.

Patient satisfaction / experience

Across studies, patients generally reported positive experiences with interventions designed to support medication adherence, though acceptability varied by approach. Videoconferencing with recovery coaches and secure pillboxes were perceived to help maintain regular dosing schedules (Janzow et al. 2022)[50], and substantial reductions in travel time and costs were noted where treatment models reduced the need for clinic attendance (Brooklyn et al. 2022[52]; Hallgren et al. 2022[53]). However, technological aids such as locked pillboxes had mixed appeal: while many demonstrated acceptance in not requesting to return the pillbox, a notable minority found the devices inconvenient or disliked the format and requested to discontinue them (Sklar et al. 2024[55]). Further, patients frequently reported pillbox malfunctioning (Kidorf, 2021[54]), highlighting the value of the pillboxes being embedded within a broader system with responsive features such as support telephone lines.

Quality of life

Not reported.

Results: Question 2

Australian guidelines

Key messages:

- Most Australian jurisdictions have not made substantive updates to their guidelines in recent years, with only Queensland and South Australia the two key exceptions
- Updated guidelines are largely consistent with New South Wales, though new approaches to risk assessment are described

National

National guidelines published across Australian jurisdictions are summarised in **Appendix 7**. We considered a wide range of documents, with the most relevant highlighted below. Most jurisdictional guidelines were published in 2016 or earlier, before the release of the 2018 NSW Clinical Guidelines on the Treatment of Opioid Dependence.[3] In several jurisdictions, there is evidence that existing guidelines are in the process of being updated, as summarised in **Table 5**. However, at the time of writing, these were not within the scope of this Evidence Check, which focused on guidelines published on or after 2020. Guidelines meeting this criterion were:

- Queensland Opioid Dependence Treatment (ODT) Guidelines[61]
- South Australian 2020 takeaway guidelines.[62]

Table 5: Summary of Australian guidelines on opioid dependence treatment

Jurisdiction	Guidelines updated	Notes
Victoria	2016 (review underway)	No clinical updates since 2020 to consider; latest update to the policy takes effect from 1 July 2023 to account for Pharmaceutical Benefits Scheme (PBS) changes commencing from 1 July 2023. All other elements of the policy remain as per the 2016 guideline

Queensland	2023	Queensland Opioid Dependence Treatment (ODT) Guidelines (2023). Key guideline for consideration given recent update
Tasmania	2014 (review underway)	Tasmanian Opioid Pharmacotherapy Program Policy and Clinical Practice Standards (TOPP) written in 2014. Document in 2022 reflects pharmacist administration of long-acting injectable buprenorphine (LAIB)
South Australia	2016 (review underway) 2020 takeaway guidelines	The Guidelines for South Australian Pharmacists Dispensing Medication Assisted Treatment for Opioid Dependence (MATOD) 2016 are the overarching guidelines, with companion pharmacist guidelines, both in the process of being updated. Practice standards for pharmacist administration of LAIB published in 2025. The 2020 takeaway guidelines[62] (with a risk assessment tool) appear to have been published in 2020 and have been considered here
Western Australia	2014	Community Program for Opioid Pharmacotherapy (CPOP)—Clinical Policies and Procedures for the Use of Methadone and Buprenorphine in the Treatment of Opioid Dependence revised in 2022. 2023 update for LAIB only in 2023
Northern Territory	2018	Code of practice: Schedule 8 Substances Volume 1: Issuing prescriptions and supplying schedule 8 substances Part 4B: Dispensing of restricted S8 substances—methadone, buprenorphine and buprenorphine / naloxone (opioid substitution treatment). Professional Practice Guideline for LAIB was developed in 2024
Australian Capital Territory	2014	ACT refers to the National Guidelines for Medication-Assisted Treatment of Opioid Dependence (2014) as guidelines for the treatment of opioid dependency

Note that several recent addenda to state and jurisdictional guidelines that focus on long-acting injectable buprenorphine were considered in this Evidence Check. A summary of how these differ from the NSW guidelines is provided below.

Queensland

The revised Queensland guidelines[61] are consistent with NSW guidelines in many respects. The updated Queensland guidelines include the introduction of a protocol for ‘micro-dosing’ of buprenorphine, allowing for induction of buprenorphine with initial low doses while tapering the other opioids. Buprenorphine is most commonly used (with LAIB being the preferred form

because of regimen simplicity), noting the improved safety profile and reduced patient medication burden compared with methadone. Of note, the prior (2018) Queensland guidelines had a ‘Risk assessment for takeaway’ table to help differentiate higher and lower risk patients, which was not included in the recently updated guidelines.

South Australia

South Australia introduced a takeaway risk assessment process with scoring to guide the level of unsupervised dosing. The assessment considers a range of factors related to safety, adherence and stability. These include risks of diversion or unsafe storage, evidence of misuse (such as hoarding, intoxication or unsanctioned drug use) and clinical concerns such as overdose history, unstable physical or mental health, or problematic alcohol use. Social and treatment-related factors are also assessed, including unstable accommodation, high-dose methadone (> 80mg) and irregular attendance.

Supervised dosing at a seven-day pharmacy is recommended during the induction and stabilisation phase. Takeaway doses may be considered in the maintenance phase, depending on the individual patient’s level of risk. Prescribers may allow takeaway doses on Sundays and public holidays for newly initiated very low-risk patients. Use of a risk assessment tool (PDF form) is encouraged to support decision making and documentation.

For buprenorphine / naloxone (Suboxone) supervised dosing is required during the stabilisation phase (typically up to three months). In the maintenance phase, takeaway doses depend on risk assessment: high-risk patients should continue supervised dosing; moderate-risk patients may receive up to four takeaways per week; and low-risk patients may have no more than 28 consecutive days unsupervised.

For methadone, the induction and stabilisation phase usually covers the first three months. In the maintenance phase, takeaway dosing again depends on risk. High-risk patients should remain on supervised dosing; moderate-risk patients may receive up to two takeaway doses per week, ideally avoiding consecutive unsupervised days; and low-risk patients may receive up to four takeaways per week, with no more than four consecutive days of take-home methadone approved.

Long-acting injectable buprenorphine (LAIB)

Most jurisdictions’ guidelines on LAIB are broadly consistent with the NSW guidelines, though there are some slight variations on direct induction where NSW guidelines explicitly state to avoid sublingual test doses, and note that there is no need to observe withdrawal before starting weekly LAIB injection. Sublocade® requires sublingual buprenorphine for at least seven days.

Most dose ranges in other LAIB state guidelines are consistent with the product information for the approved LAIB products; differences mainly concern how LAIB is started, such as whether or not direct induction can occur to weekly long-acting injectable buprenorphine, allowance for top-up sublingual dosing, and operational rules about who can administer and how medicines are handled.

As the 2024 NSW guidelines on LAIB are the most up-to-date of all jurisdictional documents, incorporating clinical learnings not available when other guidelines were published (2020–2023), it is expected that some differences exist. These differences are not surprising and given that the NSW guideline is likely to represent the most current evidence and practice, comparisons with earlier state guidelines are of limited value.

International guidelines

Key messages:

- In international guidelines, variations exist in maximum dosing limits, therapeutic hierarchies (e.g. offering alternative medications before increasing doses), and the extent of unsupervised dosing allowed.
- International guidelines often permit more liberal unsupervised dosing, particularly for buprenorphine.
- Additional medication options are available internationally, for example, second- and third-line treatment options not currently available in Australia, such as slow-release oral morphine, methadone tablets, levomethadone, injectable hydromorphone, and diacetylmorphine.

Key information published in international guidelines from countries comparable to Australia (i.e. the UK, USA, Canada and Norway) is detailed in **Appendix 8** and summarised below.

UK (England)

Guidelines reviewed

The UK guidance on oral methadone and buprenorphine was published in 2024, with recommendations about the oral / sublingual use of these drugs in the treatment of opioid dependence[63]. The National Institute for Health and Care Excellence (NICE) Technology Appraisal (TA114), published in 2007, recommended both methadone and buprenorphine as effective treatments for opioid dependence. At that time, daily supervised consumption was seen as the standard approach at initiation, with less flexibility in how doses could be provided.

The UK clinical management guidelines, known as the ‘Orange Book’, were updated in 2017 to expand on NICE’s earlier recommendations and reflect changes in clinical practice. The Orange Book provided much more detailed guidance as to assessment, induction, maintenance, supervised dosing, and the role of psychosocial support.

In 2024, the Department of Health and Social Care convened an expert group to update national guidance, focusing on the choice and use of methadone and buprenorphine in opioid substitution treatment. This update was driven by three key factors: the growing availability of new buprenorphine formulations, stronger evidence that engagement with opioid agonist

treatment is associated with reduced mortality across a range of causes, and the arrival of potent synthetic opioids in the UK, which underscored the need to retain as many people as possible in treatment. The 2024 guidance supplements, but does not replace, the Orange Book, reaffirming methadone and buprenorphine as the mainstays of treatment and highlighting the importance of patient-centred decision making. A further update is planned for 2025 to incorporate long-acting injectable buprenorphine. The desktop scan primarily drew on the 2024 update given the prior documents were published in 2007 and 2017 respectively.

Patterns of drug use and harms

In the UK in 2022 there was a rate of opioid-related deaths of about 4/100,000 people. About 70% of people in pharmacotherapy for opioid dependence treatment are on methadone; buprenorphine accounts for ~30%.[64] Drug-related deaths remain high, noting there were 709 methadone-related deaths and 46 buprenorphine-related deaths in 2023.

Treatment philosophy

Retention in treatment is a goal stated in the updated document but there is no explicit reference to the current treatment philosophy. When choosing between first-line treatments, retention (methadone) and safety (buprenorphine) are identified as trade-offs.

Health system characteristics

Opioid dependence treatment is provided through a mix of NHS and public treatment services commissioned by local councils (public health / integrated care boards (ICBs)), guided by national standards and reviews. Treatment is also provided by private prescribers, which patients must self-fund, and these private prescribers have fewer regulations.

USA

Guidelines reviewed

The Substance Abuse and Mental Health Services Administration (SAMHSA) Treatment Improvement Protocol (TIP) 63—Medications for Opioid Use Disorder for Healthcare and Addiction Professionals, Policymakers, Patients, and Families—was published in 2021. The ASAM National Practice Guideline 2020 update for the treatment of Opioid Use Disorder[65] was also reviewed, which was generally considered with the SAMHSA TIP, although additional information was included from the ASAM guideline where it differed or addressed gaps in the SAMHSA guideline. Note that Probuphine (buprenorphine implant) is referenced in these guidelines but was not included for discussion in this Evidence Check as the product has been discontinued. We also noted a recent federal ruling to make permanent the increased flexibility in unsupervised dosing that was introduced as part of the pandemic response.[66]

Patterns of drug use and harms

There is a longstanding pattern of elevated rates of opioid deaths, driven in the past 10 years by synthetic opioids (e.g. fentanyl). Stimulant use is also commonly represented in these deaths. The age-adjusted rate of drug overdose deaths increased from 8.9 deaths per 100,000 people in 2003 to 32.6 in 2022; decreasing to 31.3 in 2023.[67]

Treatment philosophy

The SAMHSA TIP 63 discusses treatment philosophy, emphasising the Guiding Principles of Recovery, including hope and individualised paths to recovery, as the foundation for comprehensive OUD treatment. The focus is on supporting recovery through person-centred care and social networks, while acknowledging medications are part of OUD treatment.

Health system characteristics

Methadone is typically restricted to federally regulated opioid treatment programs. Buprenorphine prescribing has been expanded beyond OTPs to office-based practice, community health centres and pharmacies. Federal and state layers of regulation interact and recent moves have reduced waiver restrictions for buprenorphine, meaning any licensed prescriber can now prescribe buprenorphine without requiring special permission.

Canada

Guidelines reviewed

The desktop scan primarily considered the updated 2024 Canadian Research Initiative in Substance Matters (CRISM) Guideline.[68] However, this update did not provide specific recommendations about dosing, instead directing readers to provincial guidelines. We used the 2018 CRISM Guidelines to document usual dosing practices as these summarised provincial and Centre for Addiction and Mental Health (CAMH) guidelines that many provinces follow. It should be noted that the 2018 guidance about unsupervised dosing predates the COVID-19 pandemic and does not reflect evidence or practice changes arising since that time.

The 2024 guidelines indicate a shift in the positioning of methadone and buprenorphine in the treatment of opioid dependence. Both treatments are now considered first line, reflecting a balance between safety and retention: buprenorphine is prioritised for its safer profile, while methadone is recognised for higher treatment retention, which is considered to offset the elevated mortality risk during the first month of treatment. Naltrexone for opioid dependence is not available in Canada and is therefore not addressed in the guidelines. Injectable opioid agonist treatment (iOAT) was outside the scope of the 2024 update but remains covered in a separate 2019 guideline.

Patterns of drug use and harms

Canada is experiencing a longstanding pattern of elevated opioid-related deaths. The reported annual opioid-related mortality rate of was 19/100,000 people in 2022[69], driven largely by fentanyl and synthetic opioids, with regional variation.

Treatment philosophy

There is a strong emphasis on harm reduction, including access to safer supply and iOAT in some regions. Pharmacotherapy opioid dependence treatment (methadone, buprenorphine / naloxone) are recommended as first-line treatments. Retention in treatment and reducing overdose risk is prioritised; psychosocial interventions may be offered but should not be seen as mandatory.

Health system characteristics

Canada's health system is a universal publicly funded system where residents receive medically necessary treatment through provincial and territorial health insurance plans.[70] While the federal government provides funding and sets standards, provinces and territories deliver care and administer their own insurance plans for services such as hospital and doctor visits. Methadone and buprenorphine are both used widely; slow-release oral morphine (SROM) is used off-label in some provinces. National guidance (CRISM) sets broad recommendations, but provinces / territories regulate dosing, take-homes and operational rules.

Norway

Guidelines reviewed

The National Guidelines for Medication Assisted Rehabilitation for Opioid Addiction were updated in 2022.[71] All the information we extracted is based on Google translation. Naltrexone depot injection is not approved by the Norwegian system's New Methods for the Treatment of Opioid Dependence and therefore is not mentioned in the guidelines. Details of who can prescribe pharmacotherapy for the treatment of opioid dependence in Norway are not outlined in the guidelines.

Patterns of drug use and harms

Patterns of drug use and harm have been stable in Norway, at about 6.8/100,000 deaths per year in 2022, with 80% – 90% of these from opioids, with recent increases in opioid harm.[72,73] Norway had the highest death rate of all Nordic countries in 2022, at the same level as in 2002. Most deaths are from heroin / morphine with low detection of novel synthetic opioids. A change in opioid harm was documented where there is rising mortality from prescription opioids in contrast with declining heroin-related deaths in Norway.[74]

Treatment philosophy

There is an emphasis on harm reduction combined with recovery orientation, with comprehensive care considering housing and broader wellbeing in addition to the treatment of opioid dependence.

Health system characteristics

Guidelines make reference to opioid agonist treatment being provided as part of specialist health services, with some use of primary care providers. Induction usually occurs in specialist care, with GPs and pharmacies involved after stabilisation.

Comparison between NSW Guideline and international guidelines

Medications

The core medications available in NSW were reflected in the international guidelines we examined, namely oral methadone, sublingual buprenorphine and long-acting injectable buprenorphine. Methadone and buprenorphine were typically considered first-line treatments, though there are some nuances. For example, methadone may be considered where the clinical outcomes with buprenorphine at high doses (considered to be 24 mg per day) are not optimal (e.g. patient has ongoing craving and substance use). Some differences in terms of which medications are considered first line have changed with the increasing availability of high-potency opioids. For example, in Canada, methadone and buprenorphine are both considered first-line treatments. Buprenorphine is favoured for its safety profile, but the guidelines note a risk of higher rates of treatment cessation. Methadone is now also considered first line (noting the higher risk of mortality in the first month), reflecting a shift from the prior focus on buprenorphine as the first-line treatment before the high prevalence of high-potency opioids in the illicit drug market in Canada.

Other guidelines identified additional medications that are largely used as second-line options where the clinical outcomes with first-line medications are not optimal. These medications include slow-release oral morphine (Canada and Norway), methadone tablets (Norway), levomethadone (Norway), injectable hydromorphone (Canada and Norway), injectable diacetylmorphine (Canada).

Other notable differences include lower maximum doses of 24 mg for sublingual buprenorphine compared with 32 mg in NSW. The maximum dose is 24 mg in the US, and this also considered a high dose in Norway, after which it is recommended other treatments be considered.

Methadone recommended dose ranges are typically similar to common clinical practice in Australia (60 mg – 120 mg), though stronger recommendations are made about maximum doses and considering other treatment options at this point.

Unsupervised dosing

The international guidelines reviewed often described greater levels of unsupervised dosing. Monthly collection of medications was often accessible to patients meeting required levels of stability, and buprenorphine was more routinely provided for 28–30 days at a time including from the point of initiation. Methadone was also allowed for up to 30 days unsupervised dosing, after a period of stability. Federal law in the US has made these allowances permanent after they were introduced during the COVID era. These larger amounts of unsupervised doses were already possible in the US for buprenorphine with office-based treatment. Second-line treatments such as SROM typically only allow unsupervised dosing in more exceptional circumstances.

Considerations when interpreting findings

There have been few guidelines published in Australia since 2020, limiting the scope for comparison with the NSW Guidelines. In contrast, international policies and guidelines offered more opportunities to compare and identify differing practices. For both Australian and international contexts, however, it is unclear to what extent clinical practice aligns with published guidance. In some countries, such as Canada and the US, multiple guidelines exist at both federal and state / provincial levels, suggesting potential variation in practice. Nevertheless, within individual countries, guidelines appeared relatively consistent. These comparisons identified scope for a greater range of medications than are currently options for prescribers in NSW, and greater flexibility in provision of unsupervised dosing than is reflected in the 2018 NSW Guidelines.

Discussion

This Evidence Check highlights a range of insights regarding recent evidence of the effects of unsupervised dosing (commonly referred to as takeaway doses). We considered evidence from 38 studies that explored different aspects of unsupervised or takeaway dosing in pharmacotherapy for opioid dependence treatment. In addition, we conducted a scan of recently published local and international guidelines.

Systematic review evidence indicates supervised dosing does not positively or negatively affect retention, abstinence or mortality. Unsupervised buprenorphine, including unsupervised induction, achieved comparable outcomes to supervised approaches, with clear benefits over no treatment and no major safety concerns.

There is less evidence relating to the safety of unsupervised methadone outside the context of the COVID-19 pandemic. However, during the pandemic, expanded methadone takeaway dosing was generally not associated with adverse outcomes and, in some cases, was linked to improved clinical outcomes. Epidemiological research from the UK highlighted the importance of supervised dosing with methadone, demonstrating that the introduction of supervised methadone dosing was followed by substantial declines in deaths related to overdose of methadone in both Scotland and England[4]; however, this population study cannot guide us as to the optimal level of supervised dosing for an individual patient.

Many studies and clinical guidelines emphasise that patient stability should be a primary consideration when determining suitability for takeaway dosing, as well as the number of takeaway doses provided each week or fortnight. However, clear definitions of stability or how to measure it in practice is usually lacking.

The distinction between contingent and noncontingent provision of takeaway doses is also critical. Evidence identified in this Evidence Check indicates that contingent takeaway dosing (where takeaways are linked to indicators of stability such as regular attendance or negative drug screens) is associated with better treatment outcomes. In contrast, noncontingent provision of takeaway doses may increase risks, highlighting the ongoing need for individualised assessment to guide decisions about supervised or takeaway dosing.

There was limited information available as to how such assessments are conducted in practice, or on the optimal number or frequency of takeaway doses. These aspects may therefore need to be guided by expert clinical judgement, particularly from clinicians experienced in the NSW context. International guidelines often allow more liberal unsupervised dosing, particularly for buprenorphine. Differences also exist in maximum allowable doses and therapeutic hierarchies, that include second- and third-line options such as slow-release oral morphine, methadone tablets, levomethadone, injectable hydromorphone and diacetylmorphine.

Reducing the need for daily dosing at clinics or pharmacies can offer significant benefits for people in treatment for opioid dependence, and was achieved during the pandemic with little

evidence of adverse outcomes. Consistent with this, a Canadian guideline review and evidence synthesis shows access to these doses is associated with improved autonomy, greater flexibility, stronger relationships between patients and prescribers, and better retention in treatment.[68] Patients consistently report that being trusted with unsupervised doses enhances their quality of life, reduces stigma, and supports their ability to manage work, family and other responsibilities. Importantly, risks such as diversion, misuse, or crime among those receiving take-home doses did not appear different from those on daily supervised regimens.

However, the Canadian review also reveals that access to unsupervised dosing is often inconsistent and shaped by vague or discretionary criteria about clinical stability. These criteria vary widely across jurisdictions and can be influenced by prescriber bias, leading to inequity for patients in treatment. To address these disparities, the authors of the Canadian review called for a more transparent evidence-informed and patient-centred framework that clearly defines eligibility and prioritises individual needs and circumstances. Such an approach could also inform the development of NSW guidelines, and could help ensure that the benefits of unsupervised dosing are equitably available.

The findings of this Evidence Check suggest that greater unsupervised dosing, particularly with buprenorphine, can be incorporated into opioid dependence treatment, with comparable outcomes to supervised approaches. This may have benefits for patient autonomy and engagement. A lack of consistent criteria for assessing patient stability and eligibility, and specific evidence to support the number of takeaway doses that could be suitable in different contexts presents a challenge to guiding clinical practice and to equitable access. Reviewing international practices around second- and third-line treatment options may offer opportunities to expand therapeutic choices and better meet the diverse needs of people in treatment.

Limitations

This Evidence Check was conducted using a rapid review methodology, which necessarily involved methodological constraints compared with a full systematic review. The search was limited to studies published from 2020 onwards, supplemented by targeted searches to identify key earlier evidence, and may therefore not have captured all relevant literature. We prioritised evidence from countries with health systems and treatment models comparable to NSW (e.g. Australia, the US, the UK and Canada), which may limit generalisability to jurisdictions with substantially different regulatory or service delivery contexts, or miss key evidence from other countries. The quality of included evidence was variable, with many studies being observational, of small sample size, or conducted during the unique conditions of the COVID-19 pandemic, which may not reflect usual clinical practice. The lack of studies that focused on, or even reported, the number of takeaway doses provided, or that implemented specific approaches to assess suitability for takeaways, limited the ability to draw firm conclusions or make detailed recommendations on these aspects of care. Data were often heterogeneous and inconsistently reported, further limiting opportunities for quantitative synthesis. Finally, the timeline available for the Evidence Check restricted the depth of searching, screening and data extraction, and few studies included patient-centred outcomes such as satisfaction, preference

or quality of life, limiting the ability to assess the broader impacts of supervised versus unsupervised dosing on patient experience.

Conclusion

These findings can be used to inform updates to the NSW guidelines for pharmacotherapy in opioid dependence treatment. The rapid review evidence, combined with clinical expert opinion for where evidence remains limited, can ensure that policy reflects both the best available research and practical, patient-centred considerations.

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Appendices

Appendix 1—Search strategies

Database: Ovid MEDLINE(R) <1946 to August Week 2 2025>
Date searched: 20 August 2025
Yield: 540

#	Query	Results
1	Methadone/	14,220
2	Buprenorphine/	8143
3	Buprenorphine, Naloxone Drug Combination/	639
4	Opiate Substitution Treatment/	5811
5	1 and 4	2777
6	2 and 4	2625
7	3 and 4	308
8	or/5-7 [Subject headings for M or B substitution treatment]	4429
9	Opioid-Related Disorders/	25,087
10	1 and 9 [Methadone]	4558
11	2 and 9 [Buprenorphine]	4387
12	3 and 9 [Buprenorphine, Naloxone Drug Combination]	534
13	or/10-12 [Subject headings]	7654
14	(methadone or phenadone or physeptone or phymet or dolophine or amidone or metadol or metasedin or methaddict or methadose or methex or pinadone or symoron or (methadone adj3 naloxone)).ti,ab,kf.	15,282
15	(buprenorphine or subutex or suboxone or (buprenorphine adj3 naloxone)).ti,ab,kf.	9483
16	or/14-15 [Methadone OR Buprenorphine incl Naloxone keywords]	21,828

17	("opioid agonist" or "opioid substitut*" or "opioid treatment program*" or "opioid replace*" or "opioid depend*" or "opioid use disorder*" or "opioid addict*" or "opiate agonist" or "opiate substitut*" or "opiate treatment program*" or "opiate replace*" or "opiate depend*" or "opiate use disorder*" or "opiate addict*" or "medication-assist*" or "medication* for opioid use" or "medication* for opiate use" or "methadone maintenance" or "buprenorphine maintenance" or "methadone-naloxone maintenance" or "buprenorphine-naloxone maintenance").ti,ab,kf.	24,647
18	((OAT or OST or ORT or ODT or OTP or MAT or MATOD or MOUD or MOUDs or MMT or BMT) adj20 (opioid* or opiate* or methadone or buprenorphine or methadone-naloxone or buprenorphine-naloxone)).ti,ab,kf.	3717
19	((pharmacotherap* or sublingual or monotherap* or monoproduct* or "combination therap*") adj5 (opioid* or opiate*)).ti,ab,kf.	757
20	1 or 2 or 3 or 8 or 13 or 16 or 17 or 18 or 19	39,405
21	((supervis* or observe* or witness* or "in-clinic") adj15 (dos* or dispens* or medicat* or administ* or COVID)).ti,ab,kf. [Supervised terms]	160,727
22	20 and 21	1014
23	((unsupervis* or unobserv* or unwitness* or takeaway or "take-away" or takehome or "take-home" or takehomes or "take-homes" or "self-administer*" or carry or carries or carried or flexible) adj15 (dos* or dispens* or medicat* or administ* or COVID)).ti,ab,kf.	67,896
24	((TAD or TADs or THD or THDs) adj15 (opioid* or opiate* or methadone or buprenorphine*)).ti,ab,kf.	7
25	23 or 24 [Unsupervised terms]	67,896
26	20 and 25	797
27	22 or 26 [Supervised OR Unsupervised]	1697
28	limit 27 to yr="2020 - 2025"	548
29	limit 28 to english language	544
30	**limit 29 to (journal article or "review")**	**540**

Database: Embase Classic+Embase <1947 to 2025 August 19>
Date searched: 21 August 2025
Yield: 825

#	Query	Results
1	methadone/	43,707
2	buprenorphine/	32,065
3	methadone plus naloxone/ or buprenorphine plus naloxone/	3514
4	opiate substitution treatment/	3848
5	1 and 4	1597
6	2 and 4	1427
7	3 and 4	293
8	or/5-7 [Subject headings for M or B substitution treatment]	2223
9	"opioid use"/ or "opioid use disorder"/ or opioid-related disorder/	2934
10	1 and 9 [Methadone]	440
11	2 and 9 [Buprenorphine]	682
12	3 and 9 [Naloxone Drug Combination]	108
13	or/10-12 [Subject headings]	830
14	(methadone or phenadone or physeptone or phymet or dolophine or amidone or metadol or metasedin or methaddict or methadose or methex or pinadone or symoron or (methadone adj3 naloxone)).ti,ab,kf.	25,214
15	(buprenorphine or subutex or suboxone or (buprenorphine adj3 naloxone)).ti,ab,kf.	17,083
16	or/14-15 [Methadone OR Buprenorphine incl Naloxone keywords]	36,896
17	("opioid agonist" or "opioid substitut*" or "opioid treatment program*" or "opioid replace*" or "opioid depend*" or "opioid use disorder*" or "opioid addict*" or "opiate agonist" or "opiate substitut*" or "opiate treatment program*" or "opiate replace*" or "opiate depend*" or "opiate use disorder*" or "opiate addict*" or "medication-assist*" or "medication* for opioid use" or "medication* for opiate use" or "methadone maintenance" or "buprenorphine maintenance" or "methadone-naloxone maintenance" or "buprenorphine-naloxone maintenance").ti,ab,kf.	40,780
18	((OAT or OST or ORT or ODT or OTP or MAT or MATOD or MOUD or MOUDs or MMT or BMT) adj20 (opioid* or opiate* or methadone or buprenorphine or methadone-naloxone or buprenorphine-naloxone)).ti,ab,kf.	6530

19	((pharmacotherap* or sublingual or monotherap* or monoproduct* or "combination therap*") adj5 (opioid* or opiate*)).ti,ab,kf.	1349
20	1 or 2 or 3 or 8 or 13 or 16 or 17 or 18 or 19	91,156
21	((supervis* or observe* or witness* or "in-clinic") adj15 (dos* or dispens* or medicat* or administ* or COVID)).ti,ab,kf. [Supervised terms]	286,597
22	20 and 21	2029
23	((unsupervis* or unobserv* or unwitness* or takeaway or "take-away" or takehome or "take-home" or takehomes or "take-homes" or "self-administer*" or carry or carries or carried or flexible) adj15 (dos* or dispens* or medicat* or administ* or COVID)).ti,ab,kf.	122,514
24	((TAD or TADs or THD or THDs) adj15 (opioid* or opiate* or methadone or buprenorphine*)).ti,ab,kf.	11
25	23 or 24 [Unsupervised terms]	122,515
26	20 and 25	1441
27	22 or 26 [Supervised OR Unsupervised]	3281
28	limit 27 to yr="2020 - 2025"	1179
29	limit 28 to english language	1174
30	**limit 29 to (article or "review")**	**825**

Database: EBM Reviews—Cochrane Database of Systematic Reviews <2005 to August 13 2025>
Date searched: 21 August 2025
Yield: 0

#	Query	Results
1	(methadone or phenadone or physeptone or phymet or dolophine or amidone or metadol or metasedin or methaddict or methadose or methex or pinadone or symoron or (methadone adj3 naloxone)).ti,ab.	35
2	(buprenorphine or subutex or suboxone or (buprenorphine adj3 naloxone)).ti,ab.	33
3	("opioid agonist" or "opioid substitut*" or "opioid treatment program*" or "opioid replace*" or "opioid depend*" or "opioid use disorder*" or "opioid addict*" or "opiate agonist" or "opiate substitut*" or "opiate treatment program*" or "opiate replace*" or "opiate depend*" or "opiate use disorder*" or "opiate addict*" or "medication-assist*" or "medication* for opioid use" or "medication* for opiate use" or "methadone maintenance" or "buprenorphine maintenance" or "buprenorphine-naloxone maintenance").ti,ab.	38
4	((OAT or OST or ORT or ODT or OTP or MAT or MATOD or MOUD or MOUDs or MMT or BMT) adj20 (opioid* or opiate* or methadone or buprenorphine or buprenorphine-naloxone or (buprenorphine adj3 naloxone))).ti,ab.	4
5	((pharmacotherap* or sublingual or monotherap* or monoproduct* or "combination therap*") adj5 (opioid* or opiate*)).ti,ab.	5
6	((supervis* or observe* or witness* or "in-clinic") adj15 (dos* or dispens* or medicat* or administ* or COVID)).ti,ab. [Supervised terms]	67
7	((unsupervis* or unobserv* or unwitness* or takeaway or "take-away" or takehome or "take-home" or takehomes or "take-homes" or "self-administer*" or carry or carries or carried or flexible) adj15 (dos* or dispens* or medicat* or administ* or COVID)).ti,ab.	74
8	((TAD or TADs or THD or THDs) adj15 (opioid* or opiate* or methadone or buprenorphine*)).ti,ab.	0
9	1 or 2 or 3 or 4 or 5	64
10	6 or 7 or 8	134
11	9 and 10	4
12	**limit 11 to last 5 years**	**0**

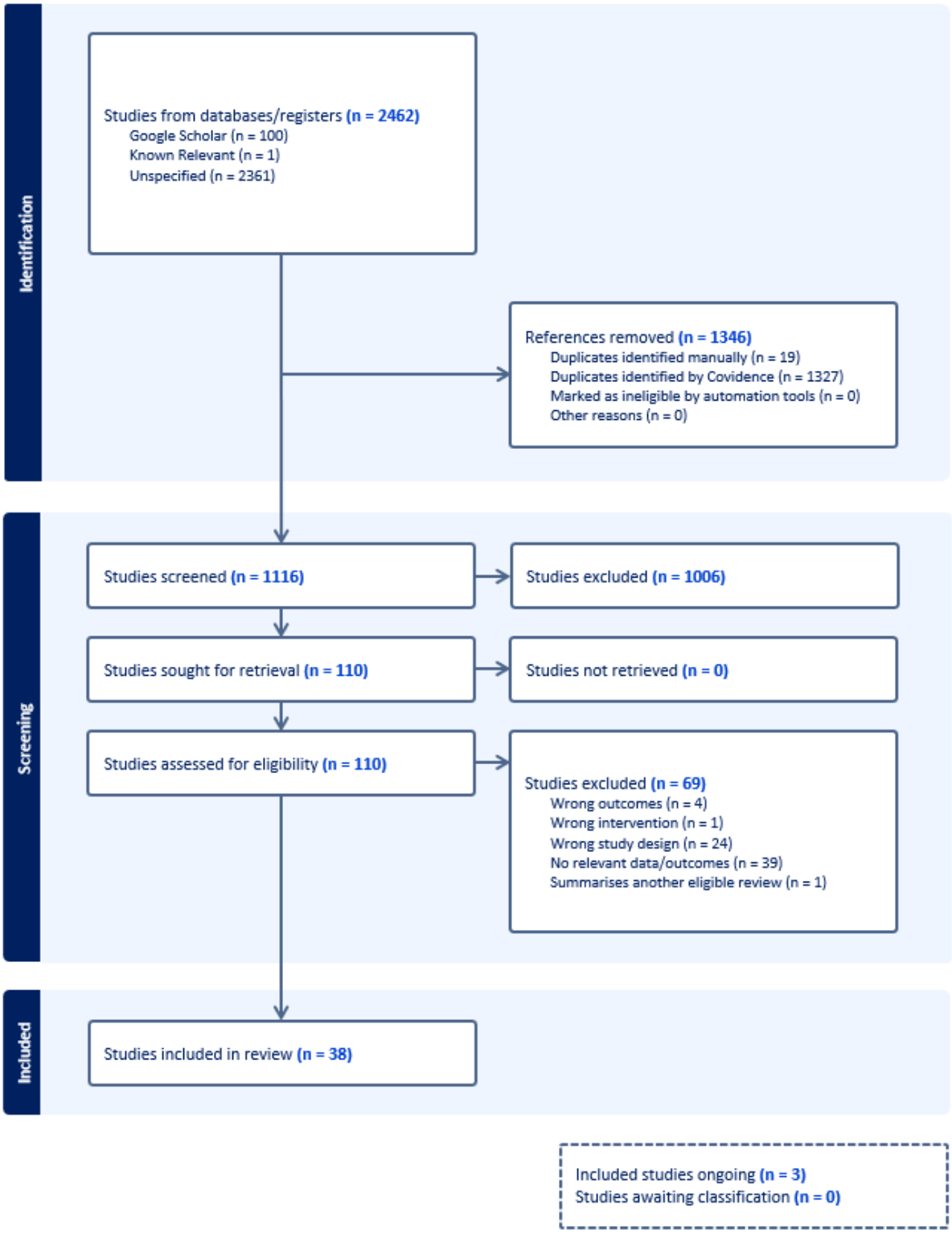
Database: Scopus
Date searched: 21 August 2025
Yield: 996

((TITLE-ABS-KEY (methadone OR phenadone OR physeptone OR phymet OR dolophine OR amidone OR metadol OR metasedin OR methaddict OR methadose OR methex OR pinadone OR symoron OR buprenorphine OR subutex OR suboxone) OR TITLE-ABS-KEY ("opioid agonist" OR "opioid substitut*" OR "opioid treatment program*" OR "opioid replace*" OR "opioid depend*" OR "opioid use disorder*" OR "opioid addict*" OR "opiate agonist" OR "opiate substitut*" OR "opiate treatment program*" OR "opiate replace*" OR "opiate depend*" OR "opiate use disorder*" OR "opiate addict*" OR "medication-assist*" OR "medication* for opioid use" OR "medication* for opiate use" OR "methadone maintenance" OR "buprenorphine maintenance" OR "methadone-naloxone maintenance" OR "buprenorphine-naloxone maintenance") OR TITLE-ABS-KEY ((OAT OR OST OR ORT OR ODT OR OTP OR MAT OR MATOD OR MOUD OR MOUDs OR MMT OR BMT) W/20 (opioid* OR opiate* OR methadone OR buprenorphine OR "methadone-naloxone" OR "buprenorphine-naloxone")) OR TITLE-ABS-KEY ((pharmacotherap* OR sublingual OR monotherap* OR monoproduct* OR "combination therap*") W/5 (opioid* OR opiate*)))) AND ((TITLE-ABS-KEY ((supervis* OR observe* OR witness* OR "in-clinic") W/15 (dos* OR dispens* OR medicat* OR administ* OR COVID)) OR TITLE-ABS-KEY ((unsupervis* OR unobserv* OR unwitness* OR "takeaway" OR "take-away" OR "takehome" OR "take-home" OR "takehomes" OR "take-homes" OR "self-administer*" OR carry OR carries OR carried OR flexible) W/15 (dos* OR dispens* OR medicat* OR administ* OR COVID)) OR TITLE-ABS-KEY ((TAD OR TADs OR THD OR THDs) W/15 (opioid* OR opiate* OR methadone OR buprenorphine*)))) AND PUBYEAR > 2019 AND PUBYEAR < 2026 AND (LIMIT-TO (DOCTYPE,"ar") OR LIMIT-TO (DOCTYPE,"re")) AND (LIMIT-TO (LANGUAGE,"English"))

Database: Google Scholar
Date searched: 21 August 2025
Yield: First 100 screened by relevance (no date limits)

methadone|buprenorphine
supervised|observed|witnessed|unsupervised|unobserved|unwitnessed|takeaway|takehome|carry|carries|flexible

Appendix 2—PRISMA diagram



Appendix 3—Quality appraisal scores

AMSTAR 2 for systematic reviews (n = 6)

Criteria	Adams 2023	Krawczyk 2023	Lee 2014	Naher 2024	Saulle 2017	Brown 2024
Did the research questions and inclusion criteria for the review include the components of PICO? (Yes/No)	Yes	Yes	Yes	Yes	Yes	No
Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	Yes	No	No	Yes	Yes	No
Did the review authors explain their selection of the study designs for inclusion in the review?	Yes	No	Yes	Yes	Yes	Partial yes
Did the review authors use a comprehensive literature search strategy?	Yes	Partial yes	Partial yes	Partial yes	Yes	Partial yes
Did the review authors perform study selection in duplicate?	Yes	No	No	Yes	Yes	No
Did the review authors perform data extraction in duplicate?	No	No	No	No	Yes	No
Did the review authors provide a list of excluded studies and justify the exclusions?	No	No	No	No	Yes	No
Did the review authors describe the included studies in adequate detail?	Yes	Yes	Yes	Yes	Yes	Partial yes
Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?	Yes	No	Yes	Yes	Yes	No
Did the review authors report on the sources of funding for the studies included in the review?	Yes	No	No	No	Yes	Yes
If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	N/A	N/A	N/A	N/A	Yes	N/A

Criteria	Adams 2023	Krawczyk 2023	Lee 2014	Naher 2024	Saulle 2017	Brown 2024
If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	N/A	N/A	N/A	N/A	Yes	N/A
Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?	Yes	No	Yes	Yes	Yes	No
Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	Yes	Yes	Yes	Yes	Yes	No
If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	N/A	N/A	N/A	N/A	Yes	N/A
Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	Yes	Yes	Yes	Yes	Yes	Yes
TOTAL SCORE:	**11/13**	**5/13**	**8/13**	**10/13**	**16/16**	**5/13**

JBI checklist for randomised controlled trials (n = 8)

Criteria	Bell 2007	Dunlop 2017	Elarabi 2021	Green 2023	Gunderson 2010	Janzow 2022	Sigmon 2023	Tsui 2021
Was true randomisation used for assignment of participants to treatment groups?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was allocation to treatment groups concealed?	No	No	No	No	No	No	No	No
Were treatment groups similar at the baseline?	Yes	Yes	Yes	Unknown	Yes	Yes	Yes	Yes
Were participants blind to treatment assignment?	No	No	No	No	No	No	No	No
Were those delivering treatment blind to treatment assignment?	No	No	No	No	No	No	No	No
Were outcomes assessors blind to treatment assignment?	No	No	No	No	No	No	No	No
Were treatment groups treated identically other than the intervention of interest?	Yes	No	Yes	Yes	Yes	No	No	Yes
Was follow-up complete and if not, were differences between groups in terms of their follow-up adequately described and analysed?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were participants analysed in the groups to which they were randomised?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were outcomes measured in the same way for treatment groups?	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Were outcomes measured in a reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the trial design appropriate, and any deviations from the standard RCT design (individual randomisation, parallel groups) accounted for in the conduct and analysis of the trial?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
TOTAL SCORE:	**7/13**	**8/13**	**9/13**	**8/13**	**9/13**	**7/13**	**8/13**	**9/13**

JBI checklist for cohort studies (n = 8)

Criteria	Binger 2020	Cousins 2017	Gomes 2022	Halgren 2022	Krenz 2022	Peles 2011	Williams 2023	Sklar 2024
Were the two groups similar and recruited from the same population?	Yes	Yes	Yes	N/A	Yes	N/A	Yes	N/A
Were the exposures measured similarly to assign people to both exposed and unexposed groups?	N/A	N/A	No	Yes	Yes	Yes	Yes	No
Was the exposure measured in a valid and reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were confounding factors identified?	Yes	Yes	No	Yes	Yes	No	Yes	Yes
Were strategies to deal with confounding factors stated?	Yes	Yes	No	Yes	Yes	No	Yes	Yes
Were the groups / participants free of the outcome at the start of the study (or at the moment of exposure)?	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Were the outcomes measured in a valid and reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Was the follow-up time reported and sufficient to be long enough for outcomes to occur?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was follow-up complete, and if not, were the reasons to loss to follow-up described and explored?	No	Yes	Yes	Yes	Yes	No	Yes	Yes
Were strategies to address incomplete follow-up utilised?	No	No	No	Yes	No	No	Yes	Yes
Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
TOTAL SCORE:	**8/10**	**9/10**	**7/11**	**9/10**	**9/11**	**6/10**	**11/11**	**8/10**

JBI checklist for quasi-experimental studies (n = 4)

Criteria	Gerra 2011	Kidorf 1994	Stitzer 1977	Stitzer 1992
Is it clear in the study what is the 'cause' and what is the 'effect' (i.e. there is no confusion about which variable comes first)?	Yes	Yes	Yes	Yes
Were the participants included in any comparisons similar?	Yes	Yes	Yes	Yes
Were the participants included in any comparisons receiving similar treatment / care, other than the exposure or intervention of interest?	Yes	Yes	Yes	Yes
Was there a control group?	Yes	No	No	Yes
Were there multiple measurements of the outcome both pre- and post- the intervention / exposure?	Yes	Yes	Yes	Yes
Was follow-up complete and if not, were differences between groups in terms of their follow-up adequately described and analysed?	Yes	Yes	N/A	Yes
Were the outcomes of participants included in any comparisons measured in the same way?	Yes	Yes	Yes	Yes
Were outcomes measured in a reliable way?	Yes	Yes	Yes	Yes
Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes
TOTAL SCORE:	9/9	8/9	7/8	9/9

National Institutes of Health (NIH) tool for before-after (pre-post) studies with no control group (n = 5)

Criteria	Kidorf 2021	Lee 2009	Lintzeris 2022	Narváez-Camargo 2025	Panwala 2023
Was the study question or objective clearly stated?	Yes	No	Yes	Yes	Yes
Were eligibility/selection criteria for the study population prespecified and clearly described?	Yes	Yes	Yes	Yes	Yes
Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	Yes	Yes	Yes	Yes	Yes
Were all eligible participants that met the prespecified entry criteria enrolled?	No	Yes	Yes	Yes	No
Was the sample size sufficiently large to provide confidence in the findings?	Yes	Yes	Yes	Yes	Yes
Was the test/service/intervention clearly described and delivered consistently across the study population?	Yes	Yes	Yes	Yes	Yes
Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	Yes	Yes	Yes	Yes	Yes
Were the people assessing the outcomes blinded to the participants' exposures/interventions?	N/A	N/A	N/A	N/A	N/A
Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	Yes	Yes	Yes	No	Unknown
Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?	No	No	No	Yes	Yes
Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?	No	Yes	No	Yes	No
If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?	Yes	No	Yes	Yes	Yes
TOTAL SCORE:	**8/11**	**7/11**	**8/11**	**9/11**	**8/11**

JBI checklist for case control studies (n = 3)

Criteria	Brooklyn 2022	Corace 2022	Hoffman 2022
Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	N/A	Yes	Yes
Were cases and controls matched appropriately?	No	No	No
Were the same criteria used for identification of cases and controls?	No	No	Yes
Was exposure measured in a standard, valid and reliable way?	Yes	Yes	Yes
Was exposure measured in the same way for cases and controls?	Yes	Yes	Yes
Were confounding factors identified?	No	Yes	Yes
Were strategies to deal with confounding factors stated?	No	Yes	Yes
Were outcomes assessed in a standard, valid and reliable way for cases and controls?	Yes	Yes	Yes
Was the exposure period of interest long enough to be meaningful?	Yes	Yes	Yes
Was appropriate statistical analysis used?	Yes	Yes	Yes
TOTAL SCORE:	**5/9**	**8/10**	**9/10**

JBI checklist for analytical cross-sectional studies (n = 4)

Criteria	Gibson 2020	Amram 2021	Barsky 2025	Haskew 2008
Were the criteria for inclusion in the sample clearly defined?	Yes	Yes	No	Yes
Were the study subjects and the setting described in detail?	Yes	Yes	Yes	Yes
Was the exposure measured in a valid and reliable way?	Yes	Yes	Yes	Yes
Were objective, standard criteria used for measurement of the condition?	Yes	Yes	Yes	Yes
Were confounding factors identified?	No	Yes	Yes	No
Were strategies to deal with confounding factors stated?	No	Yes	Yes	No
Were the outcomes measured in a valid and reliable way?	Yes	Yes	Yes	Yes
Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes
TOTAL SCORE:	**6/8**	**8/8**	**7/8**	**6/8**

Appendix 4—Data extraction tables: Systematic reviews

Table 1: Summary of study characteristics and findings (n=2)

Citation / quality score	Study aim	No of included studies / year range of search	Study setting	Primary intervention focus	Main findings	Author-stated conclusions
Lee et al. 2014[22] AMSTAR 2: 8/13	Summarise evidence as to feasibility, acceptability, safety, effectiveness, and prevalence of unobserved buprenorphine induction	10 studies No date restrictions (results range from 2007–12)	Studies were conducted in academic centres and primary care settings in the US	Unobserved buprenorphine induction vs. observed induction	• Feasibility: weak–moderate evidence supports feasibility of unobserved induction. • Safety/adverse events: weak–moderate evidence of no difference vs. observed induction. • Comparative effectiveness (week-1 successful induction): evidence insufficient to compare approaches	Patients seem to successfully induce on to buprenorphine at high rates independent of unobserved vs. observed Either observed or unobserved induction is a reasonable strategy; safety and short-term retention appear comparable in the limited literature available Prescribers should consider whether the benefits of observed induction outweigh the added convenience and comparable safety of unobserved induction
Saulle et al. 2017[8] AMSTAR 2: 16/16	Compare supervised dosing vs. unsupervised (take-home) in opioid substitution therapy (OST)	6 studies 1966 to Apr 2016	High-income settings (UK, Australia, Ireland, Italy, US); mainly outpatient; one community pharmacy trial	Supervised consumption of opioid maintenance treatment vs. unsupervised treatment	Overall, the evidence shows no clear difference between groups. Retention at 3–12 months was similar (pooled RR 0.99, 95% CI 0.88–1.12; n = 716); a 12-month observational study was consistent (RR 0.94, 0.77–1.14; n = 300). End-of-treatment abstinence was comparable (67% vs. 60%; n = 293; very low quality), as were diversion rates (5% vs. 2%; n = 293; very low quality) and adverse effects (RR 0.63, 95% CI 0.10–3.86; n = 363; very low quality). Mortality findings were inconclusive	Effects of supervision remain uncertain given limited low-quality evidence. Choice of supervised vs. unsupervised dosing should be made on a case-by-case basis, considering patient characteristics and social factors

Table 2: Summary of study characteristics and findings (*COVID-19 context*) (n = 4)

Citation / quality score	Study aim	No of included studies / year range of search	Study setting	Primary intervention focus	Main findings	Author-stated conclusions
Adams et al. 2023[6] Canada AMSTAR 2: 11/13	Assess impact of relaxed take-home dose restrictions on program effectiveness and client experience in OAT (COVID-19 context)	40 studies August – November 2022	Canada, US, UK, Australia, Bangladesh, Malaysia	Relaxation of take-home restrictions during COVID-19	Extending take-homes improved client experience—reducing stigma, exposure to unregulated drugs, and work–treatment conflicts—without evidence of increased illicit use or overdose among previously ineligible clients. Split dosing may benefit rapid metabolisers. Policy and program decisions should better incorporate patient-important outcomes, which are currently underused	Relaxing take-home restrictions improves experience and may support retention by reducing treatment burden; engage clients in care planning and include patient-important outcomes in policy / program design
Brown et al. 2024[23] AMSTAR 2**: 5/13**	To examine changes in nursing practice in OUD care during the first 2 years of the COVID-19 pandemic	N = 18 January 1, 2020 – December 31, 2021	US, Canada, China	Adaptations to OUD care among nurses implemented during the COVID-19 pandemic	Adaptations to OUD care increased telehealth and take-home of methadone / buprenorphine / naloxone. There were no clear signals of increased diversion/misuse with higher take-home doses	Highlights value of robust telehealth and flexible MOUD, including increased take-homes for appropriate patients
Krawczyk et al. 2023[24] AMSTAR 2: 5/13	To: (1) synthesise evidence of the effects of the flexibilities introduced during the COVID-19 pandemic for methadone take-home doses on the operations of OTPs, patient and provider experiences, and patient health outcomes; (2) interpret findings in the context of the US federal	29 studies Mar 2020 – Sep 2022	Primarily single / multisite OTPs (US)	Expanded federal flexibilities for methadone take-home doses	Eligibility for expanded take-homes was typically based on substance use, time in treatment, safe storage and COVID-19 risk. All studies showed increases in take-home frequency, though 14- or 28-day supplies were not always granted. Providers remained concerned about co-use (e.g. sedatives), and uptake was helped by change-management efforts such as director champions and interdisciplinary teams. Patients often reported greater autonomy and lower treatment burden, though some still faced persistent barriers	Benefits of flexible take-home policies outweigh risks when contextualised; more flexible approaches are warranted to improve access during the overdose crisis

	rulemaking process; and (3) discuss avenues by which findings can be incorporated and implemented into updated federal regulations					
Naher et al. 2024[25] AMSTAR 2: 10/13	To evaluate the efficacy of take-home methadone for patients with OUDs during public health emergencies (i.e. during COVID)	2 studies Jan 2020 – May 2024	Canada	Take-home methadone treatment during the COVID-19 pandemic (intervention duration ranged from 13–24 weeks)	High satisfaction and strong pillbox adherence in one study. General satisfaction in the other, with limited direct linkage to take-home provision. Overdoses not measured	Policy changes enabling increased take-homes show promise, but reliance on indirect measures underscores the need for more comprehensive longer-term research into health outcomes, retention and overdose prevention

Appendix 5—Data extraction tables: Primary studies

Table 1: Summary of study characteristics and findings: Studies of contingent versus noncontingent take-home doses (n = 6)

Author / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
Gerra et al. 2011[27] Italy JBI: 9/9	To test whether contingent take-home methadone with incentive procedures (vs. noncontingent take-homes), would be as effective as supervised daily consumption at reducing heroin use and methadone diversion, decreasing the frequency of criminal acts and improving psychiatric symptoms and retention rates	Multicentre observational 3 addiction services with distinct policies (supervised; contingent take-home; and noncontingent take-home) N=300 (100 / site). Participants had been heroin-dependent ≥ 4 yrs, and those with prolonged polysubstance / alcohol dependence were excluded	Unsupervised methadone (contingent and noncontingent)	Supervised daily consumption	Noncontingent unsupervised dosing approximately 3.5 times more likely to commit crime / violence, and more than six times more likely to divert their medication compared with supervised or contingent unsupervised dosing	12-mth retention: contingent 74% vs. supervised 42% vs. noncontingent 50%. Retention rates at 12 months were significantly higher in contingent take-home patients (group B, 74%) than in those with supervised daily consumption (group A, 42%) and the noncontingent take-home (group C, 50%) Risk of positive urine 5x higher in noncontingent unsupervised dose group compared with supervised group. No significant difference between positive urines in contingent unsupervised vs. supervised	Contingent take-home yields better outcomes than daily supervision. Noncontingent early take-home to non-stabilised patients was associated with a higher rate of diversion, episodes of crime and maladaptive behaviours

Author / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
Elarabi et al. 2021[26] United Arab Emirates JBI = 9/13	To estimate the clinical effectiveness of BUP maintenance with I-AAM (incentivised medication adherence and abstinence monitoring) vs. 'treatment as usual' BUP maintenance	Two-arm, single-centre, pragmatic RCT of outpatient BUP maintenance. Follow-up at 4, 8, 12 and 16 weeks United Arab Emirates N = 171; n = 141 randomised (I-AAM 70; TAU 71); adults with OUD voluntarily seeking treatment	Experimental condition was 16 weeks BUP maintenance with incentivised adherence and abstinence monitoring (I-AAM) giving contingent access to 7-day, then 14-day, then 21-day and 28-day medication supply	Treatment-as-usual (TAU) was 16 weeks BUP maintenance, with contingent access to 7-day then 14-day supply	Not reported	Follow-up rates at 4, 8, 12 and 16 weeks were 91.4%, 85.7%, 71.0%, 60.0% respectively in I-AAM and 84.5%, 83.1%, 69.0%, 56.3% in TAU. By ITT, the absolute difference in percentage negative UDS for opioids was 76.7% in I-AAM vs. 63.5% in TAU (mean difference = 13.3%; 95% CI = 3.2%–23.3%; Cohen's d =0.44;95%CI= 0.10–0.87). In I-AAM, 40 participants (57.1%) were retained vs. 33 (46.4%) in TAU (odds ratio = 1.54; 95% CI = 0.79–2.98)	Incentivised monitoring enabling larger take-home BUP increased abstinence vs. TAU; but did not appear to increase treatment retention
Kidorf et al. 1994[28] US JBI: 8/11	To determine whether take-home methadone doses can reinforce adjunct therapy attendance of drug abuse patients	Within-subject randomised design with study participants randomly assigned to receive methadone take-home dose incentives at different periods of their treatment contingent on individual therapy attendance Behavioural Pharmacology Research Unit (BPRU) Study 1 N = 10 (5 Group 1; 5 Group 2). Patients eligible if they were not earning take-homes as part of usual care incentive program, attended an average of	Contingent take homes tied to attending 2 optional therapy sessions / week for 12 weeks. Participants randomly assigned to receive methadone take-home dose incentives contingent on individual therapy attendance either during weeks 4–6 and 10–12 or during weeks 7–9 only. Patients not permitted to earn more than two take-home doses per week or to receive take-homes on consecutive days.	Contingent take-homes tied to attending 2 optional therapy sessions / week for 9 weeks. Participants randomly assigned to earn a take-home for every session attended in weeks 1–3 and 4–6 (Group 1) or weeks 1–3 and 7–9 (Group 2). In the other weeks patients not permitted to earn more than two take-home doses per week or to receive take-homes on consecutive days. Could not receive take-homes if they were alcohol-positive (via a breath test) or	Patients did not reduce their periods of increased therapy A potential disadvantage of using take-homes to reinforce therapy attendance was the risk of diversion of methadone by take-home recipients	Overall, attendance at therapy sessions substantially increased when tied to contingent take-homes. Study 1: ~75% sessions vs. 6.6% Study 1: With contingent take-homes, patients attended 75% of sessions vs. 6.6% without incentives. Across three-week blocks, they averaged 2.6 of 3 possible sessions. Drug screens were unchanged: 29% opiate-positive, 84% cocaine-positive, 31% benzodiazepine-positive Study 2: Attendance was higher when patients could earn two contingent take-homes per week rather than	Take-home incentives effectively reinforce therapy attendance; larger / contingent rewards produce stronger effects

Author / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
		1.9 routine counselling sessions and submitted an average of 37% opiate-positive urines, 85% cocaine-positive urines and 23% benzodiazepine-positive urines Study 2 N = 15 (7 Group 1; 8 group 2). Patients eligible if had been engaged in methadone treatment at BPRU for an average of 17 months and if they were using illicit drugs and submitted greater than 50% drug-positive urines during the month prior to study enrolment.	Could not receive take-homes if they were alcohol-positive (via a breath test) or appeared under the influence of drugs	appeared under the influence of drugs		one—78% vs. 51% of sessions overall. In Group 2 specifically, attendance was 71% with two per week vs. 33% with one, with a declining trend over time	
Peles et al. 2011[29] Israel JBI = 6/10	To determine whether time to first take-home privilege predicts long-term outcomes in MMT	Observational prospective study Single MMT clinic N = 657; n = 222 Never rewarded with take-homes (NEVER); 435 rewarded with 1 or more take-home doses (EVER)	Graduated privileges. First privilege after ≥ 3 months of full compliance; then +1 dose per additional month up to 5 consecutive doses. The 6th dose (once-weekly clinic attendance) requires ≥ 9 months from start plus engagement in vocational activity. Maximum 13 doses after ≥ 2 years of adherence	Not reported	Survival longer for EVER vs. NEVER group (13.2 vs. 12.3 yrs; p = 0.04). No group differences in police arrests, rehabilitation referral, hospitalisations, concluding treatment, and moving and transferring to other MMT clinics	Retention longer EVER vs. NEVER (8.6 vs. 2.2 yrs; p<0.0005). Earlier first privilege (3–6 mth) and higher max privileges (e.g. 13) associated with best retention; NEVER had higher dropout / expulsions	Patients who ever received a take-home dose tended to stay in MMT longer. Earlier first take-home (about 3–6 months) is linked with better retention and survival, making 'time to first take-home' a useful clinic quality indicator to guide and refine privilege decisions

Author / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
Stitzer et al. 1992[31] US JBI: 9/9	To determine whether contingent take-home privileges influence treatment outcomes when implemented as a general clinic policy with a group of newly admitted methadone maintenance patients	Quasi-experimental design (half cross-over) Treatment research clinic N = 53 (26 contingent; 27 noncontingent) ~ 50% of patients were on methadone maintenance and the remaining were outpatient 90-day detoxification patients	Patients could *earn* up to three methadone take-home doses per week (Tuesday, Thursday, Saturday) based on continuous abstinence. The first take-home was granted after two drug-free weeks (six consecutive negative urines); each additional take-home day required another two drug-free weeks, so the maximum (three / week) followed six drug-free weeks in total. Any positive urine within a two-week block forfeited one take-home day; regaining a forfeited day required two new drug-free weeks. Random take-home recalls checked for diversion; non-compliance triggered suspension of privileges (1 month for a first incident, 3 months for a second)	At the start of each calendar month, participants were randomly assigned to receive 0, 1, 2, or 3 take-home methadone doses per week for that entire month, irrespective of urine test results. Bottle-return and random recall procedures were identical to the contingent group. After the intervention period, 18 participants originally in this arm switched to the contingent protocol; two others dropped out after the 6-month evaluation and before the switch	A comparison of early dropouts (n = 17) and subjects who stayed through the entire 28 weeks (n = 36) revealed dropouts had significantly more urines containing any drug positive during baseline (77% vs. 58%, p < .02), significantly more urines positive for cocaine (45% vs. 26%, p < .05) and for opiates (30% vs. 10%, p<.05), and significantly more urines containing multiple drugs (39% vs. 20%, p < .01). Treatment completers and dropouts did not differ on any demographic factors	Participants who dropped out early (n = 17) entered with markedly worse **baseline** toxicology than those who completed treatment (n = 36): any-drug–positive urines 77% vs. 58% (p<.02), cocaine-positive 45% vs. 26% (p<.05), opiate-positive 30% vs. 10% (p<.05), and multiple-drug positives 39% vs. 20% (p<.01) There were no significant demographic differences between groups, indicating that higher baseline substance use—especially polysubstance use—was the key predictor of attrition, not demographics	Contingent take-homes —earned after ≥ 2 consecutive drug-free weeks—produced significantly more drug-free urines than noncontingent (random) take-homes, regardless of whether the supplemental drug was cocaine or benzodiazepines The authors recommend contingent take-homes as routine practice to promote abstinence, noting they also improve counselling attendance and can shape other therapeutic behaviours when applied systematically to clear targets
Stitzer et al. 1977[30]	To assess the efficacy of medication take-	Within-subject experiment with 5 consecutive 2-month	Contingent weekend take-homes only if counselling sessions	Noncontingent phases	Not reported	The study compared two contingent phases with three noncontingent phases	Contingent take-home privileges improve counselling

Author / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
US JBI: 7/8	home privileges as a reinforcer for methadone maintenance by making the privilege contingent upon a specific target behaviour	phases Clinic N = 16 methadone maintenance clients 13 males; 3 females	attended			(baseline, noncontingent, reversal). Weekly counselling time was higher in both contingent phases than in each noncontingent phase (all p<0.01), and counselling time in the reversal phase also exceeded baseline (p<0.05). Attendance rates showed the same pattern—contingent > noncontingent for nearly all comparisons (p<0.01; p<0.05 for the second contingent vs. final reversal). Baseline and reversal attendance did not differ significantly	attendance. When judiciously and systematically applied to clearly specified behaviours, they could be a powerful therapeutic tool in rehabilitation of patients in drug treatment programs

Table 2: Summary of study characteristics and findings: Studies of unsupervised treatment (n = 10)

Citation / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
Randomised controlled trials of unsupervised dosing (n=3)							
Dunlop et al. 2017[32] Newcastle, Australia JBI = 8/13	To determine whether patients with heroin dependence dispensed buprenorphine-naloxone weekly have greater reductions in heroin use and related adverse health effects 12 weeks after commencing treatment, compared with waitlist controls and to examine the cost-effectiveness of this strategy	An open-label waitlist RCT was conducted in an opioid treatment clinic Newcastle, Australia N = 50 adult patients with DSM-IV-TR heroin dependence (and no other substance dependence). Intervention group (n = 25), waitlist (n=25)	Take-home self-administered sublingual buprenorphine/naloxone weekly and weekly clinical review	TAU	Lower crime in the unsupervised buprenorphine group	Over 12 weeks, take-home buprenorphine reduced heroin use by ~19 days/month (95% CI −22.98 to −15.06; p<0.0001), improved mental health and quality of life, and cut adjusted costs by A$5722 (including crime). Excluding crime costs, the incremental cost per heroin-free day was A$18.24 (95% CI A$4.50–28.49). In trials comparing observed vs. unobserved dosing, retention and heroin use did not differ, and attending for observed dosing did not worsen retention	When compared with remaining on a waitlist, take-home self-administered buprenorphine-naloxone treatment is associated with significant reductions in heroin use for people with DSM-IV-TR heroin dependence
Bell et al. 2007[33] Australia JBI = 7/13	To compare the effectiveness and cost-effectiveness of unobserved vs. observed dosing of patients seeking treatment for heroin dependence	RCT and cost-effectiveness analysis. N = 119 (n=61 intervention, n=58 control) Specialist outpatient drug treatment centres in Australia treating heroin users seeking	Unobserved dosing and a weekly clinical review	Observed dosing	18 reports of diversion were documented across both arms of study	No significant differences in retention or heroin use between arms; unobserved dosing significantly cheaper (more cost-effective)	“Treatment with close clinical monitoring, but no observation of dosing, was significantly cheaper and therefore significantly more cost-effective.” (p.1899)

Citation / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
		maintenance treatment					
Sigmon et al. 2023[34] US JBI = 8/13	To evaluate TAB efficacy (1) over a longer period than previously examined, (2) with the addition of overdose education, and (3) among individuals residing in rural communities	Two parallel, 24-week randomised clinical trials. N = 100 (T1&T2: 25 TAB; 25 control) Trial 1 research clinic; trial 2 rural communities To be eligible, participants met DSM criteria for OUD, provided an opioid-positive urine test result, and were currently receiving opioid agonist treatment	Week 1: nurse-observed buprenorphine–naloxone induction with individualised titration (CINA-guided). Weeks 2–24: twelve fortnightly clinic visits with one observed dose and a urine test; all other doses taken at home using a locked dispenser within a preset 3-hour window, with the device brought to scheduled and random call-backs. Participants received nightly IVR check-ins (use, craving, withdrawal, other substances) plus twice-monthly random IVR recalls instructing them to skip the home dose and return within ~12 hours for pill count, observed dosing and urine. Baseline HIV / HCV / overdose knowledge was assessed on iPad	Control group participants did not receive medication or other services but completed the same monthly assessments with urinalysis. At each assessment, they received harm reduction supplies, condoms, a packet of community resources (e.g. substance use treatment, mental health and medical care, and housing and employment resources) and assistance contacting any resources of interest	Very high rates of treatment adherence were reported in those using unsupervised treatment with the device (i.e. 98.9 – 99.3% of doses were taken as scheduled)	Illicit opioid abstinence higher at all time points: Trial 1 85.3% vs. 24.0%, trial 2 88.0% vs. 21.3% ($p<0.001$). High satisfaction and sample submission rates	TAB is effective and acceptable. mHealth can expand access (including for rural communities) with low diversion risk

Citation / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
Observational and survey studies of unsupervised dosing (n = 3)							
Cousins et al. 2017[35] Ireland JBI = 9/10	To examine the association between supervised (vs. unsupervised) consumption and retention across multiple methadone treatment episodes	National cohort study (observational). N = 6393	Supervised methadone dosing. Typical dose 60–120 mg / day	n/a	Not reported	Over 6 years, 6393 patients had 19,715 methadone episodes. Retention showed a J-shaped relation to supervision: compared with < 20% of scripts supervised, 20–39% (HR 0.88, 95% CI 0.81–0.95) and 40–59% (HR 0.87, 0.81–0.94) were linked to longer time to discontinuation (better retention), while 60–79% (HR 1.28, 1.20–1.36) and > 80% (HR 3.59, 3.38–3.81) were linked to worse retention. Higher median doses (60–120 mg / day) and multiple treatment episodes were also associated with longer retention	Moderate supervision supports retention. Conversely, excessive supervision can undermine continuity of care

Citation / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
Binger et al. 2020[36] US JBI = 8/10	To assess (1) BUP / NAL maintenance doses and the rate of relapse in veterans with OUD, and (2) the difference in rates of relapse between daily vs. take-home dosing, tablets vs. films, time to relapse, and use of illicit substances during treatment	Retrospective cohort study. N = 128 (92% male) Veterans (18+) diagnosed with OUD who received a prescription for BUP / NAL through the substance use disorder recovery program were retrospectively evaluated (p.80)	BUP / NAL maintenance; grouped by dose (> 16 mg vs. ≤ 16 mg)	n/a	Not reported	Higher doses (> 16 mg) reduced relapse and extended time to relapse Difference in administration of dose and illicit substance use during treatment were not statistically significant (p.80)	Dose intensity mattered more than supervision for relapse in this cohort
Haskew et al. 2008[37] UK JBI: 6/8	Identify patterns / correlates of nonadherence in community methadone treatment	Cross-sectional study. N = 91 (68% male) Private room at the North Islington Drug Service, London Participants were eligible if they met DSM criteria for opiate dependence and were receiving a prescription for methadone	Pharmacy-based pick-up of methadone ≥ 5 days / week, with ~40% of doses directly supervised at the pharmacy. Mean prescribed dose 56 mg (range 10–170 mg). If a patient misses 3 days, dispensing stops until clinic review	n/a	Across the whole sample (regardless of supervision): **14%** reported giving away doses—usually to a **friend (69%)** or **partner (31%)**, most not in treatment (**56%**). **5%** reported selling doses (typically to fund heroin, crack, alcohol, private prescriptions or food), and **2%** reported exchanging doses (mainly for heroin or crack)	On the last day they used heroin, 14% had taken only part of their methadone dose—all were on unsupervised regimens—whereas most who missed a full dose that day were under supervision. Compared with full adherers, poor adherers were slightly more likely to be on a higher dose (OR 1.03) and far less likely to have 5–7 pickups / week (OR 0.20). Lack of supervised consumption strongly predicted nonadherence: OR 0.33 for partial adherers and OR 0.10 for poor adherers. The commonest nonadherence on supervision was missed pickups; on unsupervised regimens, dose-splitting—	Supervision alone doesn't ensure adherence, especially when weekend dispensing is unavailable. Because nonadherence rises with less supervision and fewer pick-ups, regular adherence reviews and stronger clinical monitoring are needed to detect and address problems

Citation / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
						often to help sleep or avoid withdrawal. 28% reported storing / saving doses in the past month, most often because they had used heroin that day	

Table 3: Buprenorphine induction (n = 4): Unsupervised

Citation / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
Green et al. 2023[60] US JBI = 8/13	To evaluate pharmacy-based medication treatment for addiction as compared with treatment as usual	RCT. N = 100 (60% male) patients with a history of OUD who were interested in receiving buprenorphine Pharmacies in Rhode Island	Pharmacists dispensed buprenorphine take-homes starting with 3–7 days, then weekly (n = 30), every 2 weeks (n = 10), or a weekly / fortnightly mix (n = 18). Naloxone was offered to all	TAU	In first month, there were 3 nonfatal overdoses (one of which was in the pharmacy group) and 3 non–overdose-related opioid emergency department visits (two of which were in the pharmacy group)	1-month retention: 89% pharmacy vs. 17% usual care	Among stabilised patients, pharmacy-based care achieved far better short-term retention
Gunderson et al. 2010[40] US JBI = 9/13	"To assess preliminary safety and effectiveness of unobserved versus observed office buprenorphine / naloxone [BUP / NAL] induction among patients entering a 12-week primary care maintenance study." p.537	RCT. N = 20 (10 observed; 10 unobserved). Participants had a substantial legal history and had received prior opioid treatment Urban, academic-affiliated primary care clinic	Observed induction at clinic. Staff stored buprenorphine–naloxone (2/0.5 mg tablets) and initiated dosing under observation when withdrawal met SOWS ≥ 17 or COWS ≥ 8. Patients started with 1–2 tablets, with additional doses per clinical response, capped at 16 mg on day 1. The target daily maintenance was 12–16 mg (up to 32 mg maximum). Patients completed daily SOWS by phone until they were on BUP / NAL and withdrawal-free for two consecutive days (SOWS < 10). Clinic visits were weekly for 4 weeks, then monthly; urine toxicology (including BUP assay) was done at every visit. Ancillary psychosocial care and self-help groups	Unobserved induction. BUP / NAL was initiated outside the office after patients received verbal and written instructions and completed the SOWS, a self-administered withdrawal scale. Patients received a prescription for BUP / NAL, usually 16 x 2 mg/0.5 mg tablets filled at a local pharmacy. They were instructed to initiate medication taking 1–2 tablets after abstaining 16 hrs or more from opioids and when the SOWS reached ≥ 17	1 precipitated withdrawal (unobserved) resolved by week 1	Week-1 induction success 6/10 per arm; 50% retained at 4 wks. Among this 50%, 3 used illicit opioids during maintenance and 7 completed the trial	Unobserved induction showed comparable safety and effectiveness to observed induction (similar induction success, stabilisation and complication rates). Larger trials needed to confirm no worse than standard office induction before broad guideline adoption

			were encouraged but not required				
Krenz et al. 2022[39] US JBI = 9/11	To evaluate patient continuation of outpatient buprenorphine therapy after induction of buprenorphine through take-home kits dispensed from the ED	Retrospective cohort analysis. N = 155 (70.3% male). Patients aged 18 years or older who received a take-home supply of buprenorphine-naloxone Urban emergency department	Buprenorphine take-home kit containing six sublingual films of 8–2 mg buprenorphine-naloxone	n/a	17 (11%) patients had a return ED visit related to opioid overdose within six months. No deaths	No significant differences between patients who received buprenorphine in the ED vs. those who underwent home induction for filling a buprenorphine prescription at 3 months or at six months	Dispensing buprenorphine take-home kits from the ED resulted in continued outpatient buprenorphine for almost 50% of patients
Lee et al. 2009[38] US JBI = 7/11	To examine the feasibility of and early outcomes associated with initiating buprenorphine at home	Case series. N = 103 (82% male) opioid-dependent adults	Home (unobserved) induction and maintenance. Day 1: Start 4 mg buprenorphine, then give 1–2 additional 4 mg doses every 1–4 h as needed (max 12 mg), guided by a pamphlet Day 2 onwards: Adjust in 4 mg increments to reach a maintenance dose. Patients phone the prescriber / coordinator on days 1–3. Issue a 7-day prescription (typically 14 × 8/2 mg BUP / NAL) to be filled at a community pharmacy. Follow-up: Day 7 (week 1), then every 1–4 weeks for the first few months, and every 4–8 weeks thereafter	n/a	No SAEs; no severe precipitated withdrawal; 5 mild–moderate buprenorphine-prompted withdrawal; 5 prolonged withdrawals (mostly methadone transfers)	Retention: 59% (12 weeks), 50% (24 weeks). Self-reported opioid use fell from 7 to 1 day a week by 12 weeks; UDS showed ongoing use in some	Home buprenorphine induction protocol was simple to implement and sustain, and resulted in no observed SAEs, few reported induction complications, and treatment retention rates consistent with previous studies
Other (n = 1)							

Gibson et al. 2020[56] UK JBI: 6/8	To examine patient safety incident reports involving opioid substitution treatment with either methadone or buprenorphine in community-based care	Mixed-methods review of national incident reports involving patients receiving community-based opioid substitution treatment. N = 2284 incident reports England and Wales	Incidents across prescribing, supervised / unsupervised dispensing for methadone, buprenorphine	n/a	Most risks of harm from opioid substitution treatment came from failure in one of four processes of care delivery: prescribing opioid substitution (n = 151); supervised dispensing (n = 248); non-supervised dispensing (n = 318); and monitoring and communication (n = 1544)	Not reported	Risks of harm in delivering opioid substitute treatment arise out of failures in four processes: prescribing opioid substitution, supervised dispensing, non-supervised dispensing and monitoring and communication

Table 4: Summary of study characteristics and findings: Studies conducted during the COVID-19 pandemic (n = 9)

Citation / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
Amram et al. 2021[42] US JBI score: 8/8	To evaluate the effects of the SAMHSA exemption on methadone adherence and OUD-related outcomes	Cross-sectional observational study. N = 183 patients (58% female) on stable methadone dosing for 9 mths prior Methadone clinic, Spokane, Washington, US	Take-home methadone doses during the COVID-19 exemption period	n/a	ED visits fell (40.4%→30.6%). Transport barriers tied to higher OD-related ED visits	No association between more take-homes and nonadherence, ED visits or OD events	More take-homes did not worsen outcomes for stable clients
Barsky et al. 2025[43] US JBI score: 7/8	To examine whether the Massachusetts take-home methadone policy was associated with changes in post-release initiations of medications for opioid use disorder and opioid overdoses among recently released people, including rural residents	Retrospective, cross-sectional study. N = 80,396 (85% male). Individuals aged 18+ released from prison Massachusetts	Expanded methadone take-homes. Buprenorphine, methadone and extended-release naltrexone within 7 days of release from prison	n/a	Statistically significant difference in the rate of overall opioid overdoses between the pre- and intra-pandemic periods (2185 [3.5%] vs. 547 [3.2%]; p=0.046). The rate of fatal opioid overdose was higher before than after the pandemic (702 [1.1% of pre-pandemic sample] vs. 102 [0.6% of intra-pandemic sample]; p<0.001. The rate of non-fatal opioid overdose was similar before and after the pandemic (1483 [2.4%] vs. 445 [2.6%]; p=0.101)	Methadone initiation post-release increased	Take-home methadone policy enabled some people released from incarceration to avoid the risk of opioid overdoses that existed during the pandemic

Citation / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
Corace et al. 2022[44] Canada JBI = 8/10	To evaluate the changes in unsupervised OAT dosing after the release of the Ontario COVID-19 OAT Guidance based on patients' and prescribers' reports	Case series (self-reported before and after study). N = 402 (54% male). 18+ being prescribed OAT Ontario, Canada	Unsupervised OAT dosing	n/a	During the pandemic, **57%** of patients reported receiving extra unsupervised (take-away) OAT doses. Those who received extra doses were more likely to **share or trade** them, but they did **not** report higher rates of **lost or stolen doses**, **early refills**, **overdose**, **ED visits**, or **hospital admissions** than patients who did not receive extra doses	Patients and prescribers viewed expanded unsupervised dosing positively—reporting better relationships and greater openness—and many (especially prescribers) supported keeping flexible take-home policies after the pandemic	Results support the case for re-evaluating traditional OAT delivery—especially rules about unsupervised doses—and for adopting policies that reduce access barriers both during and after the pandemic. Ongoing flexibility in dosing (including take-homes) is key to patient-centred care for people with OUD
Gomes et al. 2022[45] Canada JBI = 7/11	To evaluate whether increased take-home doses of OAT early in the COVID-19 pandemic was associated with treatment retention and opioid-related harm	Retrospective propensity-weighted cohort study. N = 21,297. Methadone and buprenorphine / naloxone recipients	Increased take-home doses of OAT	No change in take-home doses of OAT	Among people on daily-dispensed OAT pre-COVID, starting take-homes did not increase mortality: all-cause 1.5% vs. 1.3% / person-year; HR 1.16 (95% CI 0.62–2.16) and opioid-related 0.6% vs. 0.5% / person-year; HR 1.26 (0.48–3.33); mortality analyses in the buprenorphine / naloxone subgroup were not possible (≤ 5 deaths). For those on weekly-dispensed OAT, extending take-homes was not associated with higher opioid overdose 1.4% vs. 1.8%; HR 0.80 (0.50–1.28), all-cause mortality 1.3% vs. 0.8%; HR 0.74 (0.43–1.27), or opioid-related death ≤5 vs. 0.3%; HR 0.48 (0.16–1.45); opioid-related deaths were too few in the buprenorphine / naloxone	For people on methadone with daily dispensing before COVID, starting take-homes improved outcomes: lower opioid overdose (6.9% vs. 9.5% / person-year; HR 0.73, 95% CI 0.56–0.96), lower treatment discontinuation (51.0% vs. 63.6%; HR 0.80, 0.72–0.90), and fewer interruptions (19.0% vs. 23.9%; HR 0.80, 0.67–0.95). For buprenorphine / naloxone with daily dispensing, initiating take-homes showed no significant changes in overdose, discontinuation or interruptions. Among those on methadone weekly, extending to ≥ 13 take-homes reduced discontinuation (14.1% vs. 19.6%; HR 0.72, 0.62–0.84)	Increasing OAT take-home doses—vs. no change—was linked to lower treatment interruption and discontinuation across most patient groups, with no significant rise in opioid overdoses over 6 months. Given study design, results should be interpreted with caution

Citation / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
					subgroup for analysis	and interruptions (5.1% vs. 7.4%; HR 0.69, 0.53–0.90). For weekly buprenorphine / naloxone, extended take-homes did not significantly change overdose, discontinuation or mortality, but did reduce interruptions (9.5% vs.12.9%; HR 0.74, 0.56–0.99)	
Hoffman et al. 2022[46] US JBI: 9/10	To assess patients' responses to enhanced access to take-home methadone in two opioid treatment programs (OTPs) that served five Southern Oregon rural counties	Mixed-methods study. N = 377 (49% female). Methadone patients who had discontinued treatment Rural opioid treatment programs in southern Oregon, US	Methadone take-home doses	n/a	Not reported	Across the cohort, 65% were in care at baseline and 47% of the initial cohort remained at study end. After COVID policy relaxation, take-home dosing increased ~15% (95% CI 0.11–0.19; p<.001). For patients > 180 days in care, monthly take-homes rose from median 8→13 (p=.011) without changes in UDT positivity or retention. Patients < 90 days did not receive more take-homes and were more likely to discontinue (13% pre- vs. 26% post-COVID; p=.047). Those 90–180 days also saw no take-home increase and had higher UDT opioid positivity (19%→33%; p=.041). Each 1% increase in take-homes above expected was linked to 3% lower odds of discontinuation (aOR 0.97, 95% CI 0.95–0.99; p=.003) and lower UDT opioid positivity (B=−0.12, 95% CI −0.21 to −0.04;	Relaxing methadone take-home rules increased take-home doses, improved retention, and reduced UDT opioid positives among clinically stable patients. Qualitative data suggest fewer restrictions are feasible, preferred, and not linked to safety or public-health harms. By contrast, patients in treatment < 90 days—who did not receive more take-homes—were more likely to discontinue post-COVID, likely due to pandemic-related disruptions rather than dosing policy

Citation / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
						p=.005). Interviews described benefits of greater trust / responsibility, less travel, enabling work and recreation, and fewer triggers from unstable peers	
Lintzeris et al. 2022[7] Australia JBI = 8/11	To examine treatment conditions and patient outcomes in the 5 months before and after the introduction of COVID-19 related OAT changes	Pre-post study. N = 429 (33% female). (355 remained in treatment; 74 discharged during follow-up). Patients who were enrolled in OAT Public clinic and community dosing sites South Eastern Sydney Local Health District, Australia	Expanded take-away dosing and increased use of depot buprenorphine	n/a	Injecting prevalence was unchanged, but median injecting days fell from 5 to 4 (n = 124; p=0.010). Cannabis use rose modestly (33% to 38%; p=0.028). At the individual level, 22% showed increased use of higher-risk substances (opioids, alcohol, benzodiazepines, stimulants), more often among those with fewer take-home doses (TADs)	Over five months, retention was high (only < 5% dropped out) with two unrelated deaths and one COVID-19 case. Among the 74 discharges, 24% were imprisoned, 22% transferred, 23% withdrew with staff consent, and 28% left against advice/without notice. Substance use generally improved: fewer patients used opioids (p=0.033) and benzodiazepines (p=0.014), and among opioid users, median days fell from 4 to 2 (p=0.001); cannabis use increased. In unadjusted analyses, pharmacy dosing had fewer deteriorations than clinic dosing (17.7% vs. 29.7%; OR 0.51), and deterioration fell as take-away doses (TADs) increased (32.5% with none → 12.6% with 6+; OR 0.30). In multivariable models, only 6+ TADs / week remained protective (OR 0.27 vs. none), and Aboriginal or Torres Strait Islander status was associated with lower	Preliminary data indicate the COVID-era model remained safe and effective: more take-away doses (TADs) were not linked to increased substance use. The results support reducing supervised dosing for many patients, but caution is warranted since the study didn't assess non-medical use of TADs or harms from diversion

Citation / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
						odds of deterioration (OR 0.39). Homelessness decreased from 12% to 5% (p<0.001); other social indicators were unchanged	
Narváez-Camargo et al. 2025[47] Spain JBI = 9/11	To analyse the changes of in-person and hybrid treatment activity and extended dosing across the phases and whether this flexibility was related to treatment dropout	Retrospective observational study based on data. N = 10,609 (86.9% male). Participants were OUD outpatients receiving methadone treatment Treatment centres: Andalusia, Spain	Hybrid care with extended take-home dosing	n/a	Not reported	Hybrid care (in-person + telehealth) significantly reduced dropout vs. in-person only. Flexible dispensing alone wasn't linked to dropout, but combined with hybrid care it further lowered risk (OR 0.56, 95% CI 0.33–0.93). Hybrid care was more common in patients with anxiety / personality disorders; extended take-homes were more frequent among employed or HIV-positive patients. Both approaches were more accessible to people with less frequent prior substance use. Weekly pickup (7–14 days) was the preferred regimen, daily dosing fell (23.8% – 18.5%) and > 14-day intervals rose (11.3% – 19.3%). Longer dispensing intervals were more common among the employed (26% – 30% vs. 12% – 13%), those with lower prior use (<1 day / week; 20.7% – 28.1% vs. 12.9% – 15.1%), and at higher methadone doses (especially pre-pandemic). Dispensing categories: < 7	Hybrid care improves flexibility and access but isn't universally suitable. For patients with complex needs (e.g. comorbid mental health disorders), it should be offered as a tailored option—reinforcing that **one size doesn't fit all** and treatment should match individual complexity

Citation / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
						days, 7–14 days, > 14 days	
Panwala et al. 2023[48] US JBI = 8/11	To assess the impact of an exemption to existing US regulation of methadone maintenance therapy after the onset of the COVID−19 pandemic that permitted increased take-home doses	Pre-post study. N = 187 (58% female). Participants were 18+ receiving methadone and remained in treatment and on stable methadone dosing for 142 working days prior. Spokane opioid treatment program (OTP)	Expanded methadone take-home doses under the SAMHSA COVID-19 exemption	n/a	Not reported	Take-home methadone increased by 93% after the SAMHSA exemption (102.6 to 198.4 doses). Urine toxicology positivity rose across opioids—6-acetylmorphine 26.2% to 36.3%, codeine 32.6% to 40.6%, hydromorphone 34.2% to 44.2%, morphine 39.5% to 48.1%, fentanyl 8.0% to 14.4%—all p<.001. Testing frequency was similar (5.23 vs. 5.82 UDTs/person) pre- and post-exemption	Expanding take-home methadone during COVID-19 was not associated with increased illicit opioid use, indicating the dosing change did not worsen misuse
Williams et al. 2023[49] US JBI = 11/11	To compare retention in treatment, opioid use, and adverse events among patients newly entering methadone maintenance in the post-COVID period in comparison with unexposed controls	Retrospective observational cohort study. N=821. 58.9% male) Licensed Opioid Treatment Programs, US	Expanded early take-home methadone doses	Pre-COVID, 1 year-ago cohort	Expanded early take-home methadone (up to 14–28 days) did not increase dropout (time-to-discontinuation HR 1.02, 95% CI 0.81–1.27) or adverse events (ED / hospitalisation / overdose, p = 0.46), though opioid use was higher post-COVID than pre-COVID (64.8% vs. 51.1%, p < 0.001). Increases in take-homes occurred regardless of demographics	Six-month retention was the same post- and pre-COVID (60.0% vs. 60.1%). Cohorts were otherwise similar at baseline, with the only difference being more psychostimulant use disorder post-COVID (32.9% vs. 25.7%, p=0.02). Clinics tended to grant more take-homes to patients whose morphine / codeine / heroin use decreased, and fewer to those with no change (less than both improving and worsening groups)	Relatively modest increases in take-homes for patients newly beginning treatment were identified. Patients had equivalent retention in care at 6 months and equivalent risk of adverse events while in care despite slightly higher rates of opioid use at the group level, even among sites with routine take-homes exceeding 7–14 days early in treatment

Table 5: Summary of study characteristics and findings: Remote supervision (n = 6)

Citation / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
Janzow et al. 2022[50] US JBI = 7/13	To examine "the feasibility, usability, and acceptability of MySafeRx, during office-based B / N [buprenorphine / naloxone] treatment	Randomised controlled trial. N = 27 (13 treatment; 14 TAU). Participants eligible if positive illicit opioid screen in the 30 days prior or missed opioid toxicology screens with suspected illicit drug use as indicated by the clinical provider Office-based opioid treatment (OBOT) programs	MySafeRx—a mobile platform integrating motivational coaching, adherence monitoring and electronic dispensing intervention. Participants received six weeks of mobile recovery coaching and medication adherence monitoring via the MySafeRx program and corresponding mobile Android application. After completion of 6 weeks in MySafeRx, participants were offered an optional two additional weeks of study participation for a gradual taper with reduced frequency of MySafeRx support at the conclusion of the initial six weeks, for a potential total of 8 weeks of study intervention	Treatment-as-usual participants involved the continuation of typical OBOT BUP / NAL treatment	"MySafeRx gave clinicians clearer, day-to-day insights, revealing illicit use, socioeconomic barriers to care, and frequent medication sharing (especially among siblings). Adherence, particularly the locked e-pill dispenser, had limited, highly context-dependent acceptability	Exploratory analyses were underpowered and showed no significant urine toxicology differences vs. standard care. Mobile recovery coaches verified buprenorphine–naloxone self-administration for the 12 intervention participants on ~64% of study days (below the planned 71%). Usability was good (SUS 78.4 overall; 72.5 among men), and participants agreed it helped them dose more regularly (mean 4.1/5)	"The daily monitoring plus locked e-dispenser model had low appeal among patients already struggling with adherence. Even so, coach and staff reports flagged important treatment issues in real time, enabling clinicians to adjust care promptly

Citation / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
Tsui et al. 2021[51] US JBI = 9/13	To assess feasibility of using video directly observed therapy (DOT) for patients initiating buprenorphine, and whether it is associated with better OUD outcomes compared with TAU	RCT. N = 78 (39 intervention; 39 TAU). Patients with OUD initiating buprenorphine treatment Office-based opioid treatment (OBOT) programs in primary care and mental health clinics in Seattle, US	Video directly observed therapy (DOT) where participants uploaded at least one video / day of themselves taking their buprenorphine medication for 12 weeks showing placement of their medication sublingually and recording for three minutes	Standard care provided at clinic, which included weekly and / or biweekly visits with nurse care managers or providers with UDT	The majority of serious adverse events (SAEs) were hospitalisations, either expected (i.e. for reasons related to substance use or substance use treatment) or unexpected; no SAE/AEs were deemed related to the study intervention. One death occurred in the intervention arm after the 12-week study intervention period	Video DOT did **not** outperform standard care. Opioid-negative urines were 50% with vDOT vs. 64% with TAU (RR 0.78, 95% CI 0.60–1.02; p=0.07), and remained non-significant after excluding UDTs missing for incarceration / hospitalisation/ COVID (RR 0.82; p=0.10). Engagement was similar (RR 0.84; p=0.20). At week 12, stimulant use was lower with vDOT (29% vs. 43%), but no significant differences were seen in buprenorphine adherence (self-report or UDT) or patient satisfaction; other exploratory outcomes were likewise not statistically different	Video DOT did not improve illicit opioid use or treatment engagement vs. standard care, though it can verify buprenorphine adherence for some patients and was used variably. Future work should test vDOT with incentives (e.g. payments or fewer in-person visits) to understand if effectiveness improves
Brooklyn et al. 2022[52] US JBI = 5/9	To explore whether a novel treatment platform using a video directly observed therapy (vDOT) smartphone app and a secure medication dispenser to support adherence with take-home doses of methadone or buprenorphine reduces time and cost of travel, and	Case series. N = 58.Adults in an OTP experiencing travel hardship, access to Wi-Fi or cellular network, and having an iPhone 4S or Android 4.0 or greater	Patients received clinic-dispensed methadone or buprenorphine packaged in a locked electronic pill dispenser plus a smartphone vDOT app, with counselling and urine drug testing. Doses were supplied for 7 days at a time. The small dispenser held up to 5 buprenorphine tablets (≤ 24 mg) or low-dose methadone (< 51 mg); the large dispenser held up to 15 x 10 mg	n/a	Only 10 (0.063%) participants showed signs of medication noncompliance with 1 (0.0064%) showing an overt attempt at diversion	93% of participants engaged in prosocial activities, median cost saved per week was $72, median travel time saved was 5.5 hours a week and 98% of participants were in treatment 12 months post intervention	A secure electronic dispenser improved confirmed medication ingestion, and pairing it with vDOT appears to be a promising platform for supporting adherence

Citation / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
	increases retention		methadone tablets (≤ 150 mg) (p.311)				
Hallgren et al. 2022[53] US JBI = 9/10	To assess the acceptability and feasibility of the pilot program, and to compare clinical outcomes and service usage of patients with a matched control	Retrospective observational cohort study. N = 66 (64% male). 33 intervention; 33 control. Participants eligible if receiving methadone treatment Multisite opioid treatment program (OTP) agency, US	A clinical pilot program of video observation of methadone take-home dosing via smartphone	Patients who did not participate in the pilot program	One participant had ≥4 consecutive days of methadone disruption; no participants or matched controls died or had known overdoses	At baseline, most pilot participants had 3–4 take-homes a week (70%), whereas matched controls already had more take-homes (27% had 6 a week; 27% had 13 per 2 weeks). During the two-week pilot, participants had take-homes available on 41.9 days and uploaded accepted videos on 37.1 days (88.6% of expected). They accrued far more observed doses (in-person or video) than controls (53.15 vs. 16.64 days; 95% CI 31.31–41.72), almost entirely because of video observation. All pilot and control patients were retained for 60 days, but 61% of pilot participants graduated to increased take-homes vs. 0% of controls	"Video observation of methadone take-home doses was acceptable and feasible, and it helped confirm adherence, enabling clinics to safely expand take-home privileges. Wider use could reduce treatment barriers, lower overdose and infection risks, and make methadone care more flexible for suitable patients
Kidorf et al. 2021[54] US JBI: 8/9	To describe the use of the commercially available Medminder electronic pillbox at a community substance use disorder treatment program to safely increase the number of methadone take-home doses administered during the	Case series. N = 42. Participants with opioid and other substance use disorders deemed vulnerable to take-home mismanagement or more severe symptoms from COVID-19 infection were offered the pillbox ATS program at a community-	Medminder electronic pillbox that contains 28 cells that lock independently and open during preprogrammed time windows. Program staff can reprogram individual cells to open outside of programmed times when clinically indicated	n/a	Five patients were removed from the electronic pillbox because of tampering alerts ('unscheduled refill' or 'empty cup removed'). All reverted to standard liquid dosing with closer onsite monitoring. No overdoses occurred. Overall, take-homes rose from 11 to 25.6 per month—an average increase of ~14–15 doses a	The increase [in take-homes] varied within patient subgroups, with Current Use patients receiving larger monthly increases (19 more take homes per month) than Mismanagement or Med/Cog patients (about 12 and 8 more take-homes per month, respectively), though they were required to attend the clinic more frequently in response to their current use Twelve patients were suspected of pillbox tampering, and repeated alerts led to loss of pillbox privileges. Current Use patients made ~half of 31 support-line calls, mainly for device malfunctions, opening a compartment	The pillbox's safety features, monitoring and responsive support line improved communication and helped prevent mismanagement of take-home doses. Although limited by a single-site, retrospective design and short follow-up, the study offers preliminary evidence that the pillbox is acceptable and feasible for vulnerable patients, reducing COVID-19 exposure risk and take-home

Citation / country / quality score	Study aim	Study design / setting / sample characteristics	Intervention	Control (if applicable)	Safety outcomes	Effectiveness outcomes	Author-stated conclusions
	COVID-19 pandemic	based centre, US			month after pillbox assignment	outside the dosing window, or resetting the window because of schedule changes	mismanagement
Sklar et al. 2024[55] US JBI = 8/10	To evaluate the feasibility and acceptability of a commercially available electronic pillbox to safely administer methadone take-home tablets in a large community-based OTP	Retrospective observational study. N = 24 (54% male) Community-based OTP, US	Medminder 'Jon' pillbox-supported methadone take-homes. An electronic dispenser with independently locking compartments. Take-home quantities were risk-stratified: clinically stable / medically vulnerable patients were enhanced to ~13 take-homes per visit, while those at higher mismanagement risk received ~6/visit	n/a	About half (54.2%) of participants triggered possible tampering alerts (e.g. 'unscheduled refill', 'empty cup removed'), averaging 0.83 episodes a month; 2 participants (8%) were removed for suspected tampering	More than half the participants (62.5%) missed at least one methadone dose. Overall, participants only missed M = 0.76 (SD = 1.1) doses per month Three participants (13%) were removed from the study because of repeated technical problems that could not be resolved About half (54%) demonstrated acceptance by not requesting to return the pillbox (M = 41.9 weeks on pillbox; SD = 24.3); however, four of these participants transferred to other facilities and two passed away Six participants (25%) asked to stop using the pillbox because of reported inconvenience and / or disliking the tablets (M = 4.5 weeks on pillbox; SD = 4.7). These participants experienced a reduction in take-home privileges	Overall, this study provides evidence of the generalisability of electronic pillbox use for patients receiving methadone. The electronic pillbox provides a promising pathway to support safe administration of methadone take-homes across a range of methadone administration practices and patient profiles

Appendix 6—Other studies of interest

Table 1: Ongoing studies of interest (n = 3)

Citation
Cousins G, Durand L, Bennett K, O'Hara A, Crowley D, Lyons S, Keenan E. Impact of guidance issued during COVID-19 to expand take-home doses of opioid agonist treatment (OAT) in Ireland: protocol for a population-based analysis of prescribing practices and patient outcomes 2018 to 2023. HRB Open Res. 2025 Apr 7;8:32. doi: 10.12688/hrbopenres.14044.2. PMID: 40443921; PMCID: PMC12120409[75]
Hossain MB, Guerra-Alejos BC, Kurz M, Min JE, Karim ME, Seaman S, Bach P, Platt RW, Gustafson P, Bruneau J, McCandless L, Socías ME, Nosyk B. Comparative effectiveness of methadone take-home dose initiation in British Columbia, Canada: protocol for a population-based retrospective cohort study using target trial guidelines. BMJ Open. 2025 Mar 5;15(3):e095198. doi: 10.1136/bmjopen-2024-095198. PMID: 40044208; PMCID: PMC12107636[76]lu
Luderer H, Enman N, Gerwien R, Braun S, McStocker S, Xiong X, Koebele C, Cannon C, Glass J, Maricich Y. A Prescription Digital Therapeutic to Support Unsupervised Buprenorphine Initiation for Patients With Opioid Use Disorder: Protocol for a Proof-of-Concept Study. JMIR Res Protoc. 2023 Jan 20;12:e43122. doi: 10.2196/43122. PMID: 36662568; PMCID: PMC9898828[77]

Table 2: Excluded studies of interest (*epidemiological studies with indirect evidence*) (n = 18)

Title	Author, year	Doi / link
Impact of supervision of methadone consumption on deaths related to methadone overdose (1993–2008): analyses using OD4 index in England and Scotland	Strang 2010	https://scholar.google.com/scholar?cites=3956963373626626357&as_sdt=2005&sciodt=0,5&hl=en
Methadone Take-Home Policies and Associated Mortality: Permitting versus Non-Permitting States	Harris 2024	10.1177/29768357241272379
Methadone-involved overdose deaths in the US before and after federal policy changes expanding take-home methadone doses from opioid treatment programs	Jones 2022	https://scholar.google.com/scholar?cites=6413766004975512426&as_sdt=2005&sciodt=0,5&hl=en
The relationship between take-away methadone policies and methadone diversion	Ritter 2005	10.1080/09595230500263939
Changes in methadone program practices and fatal methadone overdose rates in Connecticut during COVID-19	Brothers 2021	https://scholar.google.com/scholar?cites=13216395760561554224&as_sdt=2005&sciodt=0,5&hl=en
COVID-19 and the Opioid Epidemic: An Analysis of Clinical Outcomes During COVID-19	Ezie 2022	10.1177/11782218221085590
COVID-19-related flexibility in methadone take-home doses associated with decreased attrition: Report	Kawasaki 2023	10.1016/j.josat.2023.209164

Title	Author, year	Doi / link
from an opioid treatment program in central Pennsylvania		
Critical incidents in Colorado's opioid treatment programs: A comparison of the COVID-19 pandemic to previous years	Bortz 2024	10.1016/j.josat.2024.209342
Evaluating interventions to facilitate opioid agonist treatment access among people who inject drugs in Toronto, Ontario during COVID-19 pandemic restrictions	Bouck 2022	10.1016/j.drugpo.2022.103680
Examination of methadone involved overdoses during the COVID-19 pandemic	Kaufman 2023	10.1016/j.forsciint.2023.111579
Investigating heterogeneous effects of an expanded methadone access policy with opioid treatment program retention: A Rhode Island population-based retrospective cohort study	Allen 2025	https://dx.doi.org/10.1093/aje/kwaf092
Methadone and buprenorphine-related deaths among people prescribed and not prescribed Opioid Agonist Therapy during the COVID-19 pandemic in …	Aldabergenov 2022	https://scholar.google.com/scholar?cites=6777020664864347641&as_sdt=2005&sciodt=0,5&hl=en
Methadone exposures reported to poison control centers in the United States following the COVID-19-related loosening of federal methadone regulations	Welsh 2022	10.1016/j.drugpo.2022.103591
Methadone-involved overdose deaths in the United States before and during the COVID-19 pandemic	Kleinman 2023	10.1016/j.drugalcdep.2022.109703
Methadone-involved overdose deaths in urban and rural communities before and after the public health emergency flexibilities for methadone take-home doses	Harris 2025	10.1016/j.dadr.2025.100339
Racial, Ethnic, and Sex Differences in Methadone-Involved Overdose Deaths before and after the US Federal Policy Change Expanding Take-home Methadone Doses	Harris 2023	10.1001/jamahealthforum.2023.1235
Reimagining patient-centered care in opioid treatment programs: Lessons from the Bronx during COVID-19	Joseph 2021	10.1016/j.jsat.2020.108219

Table 3: Excluded studies of interest (*other*) (n = 39)

Title	Author, year	Doi / link
A meta-analysis comparing buprenorphine to methadone for treatment of opiate dependence	Barnett 2001	10.1046/j.1360-0443.2001.9656834.x
An international comparative policy analysis of opioid use disorder treatment in primary care across nine high-income jurisdictions	Chiu 2024	10.1016/j.healthpol.2024.104993
Barriers and facilitators to opioid agonist treatment (OAT) engagement among individuals released from federal incarceration into the community in Ontario, Canada	Russell 2022	10.1080/17482631.2022.2094111
Changes to methadone maintenance therapy in the United States, Canada, and Australia during the COVID-19 pandemic: A narrative review	Panwala 2023	10.1016/j.josat.2023.209086
Client preferences for the design and delivery of injectable opioid agonist treatment services: Results from a best–worst scaling task	Metcalfe 2024	10.1111/add.16620
Comparing methadone policy and practice in France and the US: Implications for US policy reform	Englander 2024	10.1016/j.drugpo.2024.104487
Consensus recommendations for opioid agonist treatment following the introduction of emergency clinical guidelines in Ireland during the COVID-19 pandemic: A national Delphi study	Durand 2022	10.1016/j.drugpo.2022.103768
Cumulative barriers to retention in methadone treatment among adults from rural and small urban communities	Pasman 2022	10.1186/s13722-022-00316-3
'Diversion' of methadone or buprenorphine: 'harm' versus 'helping'	Havnes 2013	10.1186/1477-7517-10-24
Economic analysis of out-of-pocket costs among people in opioid agonist treatment: A cross-sectional survey in three Australian jurisdictions	Tran 2022	10.1016/j.drugpo.2021.103472
Examining inequities in access to opioid agonist treatment (OAT) take-home doses (THD): A Canadian OAT guideline synthesis and systematic review	Russell 2024	10.1016/j.drugpo.2024.104343
Experiences with take-home dosing in heroin-assisted treatment in Switzerland during the COVID-19 pandemic—Is an update of legal restrictions warranted?	Meyer 2022	10.1016/j.drugpo.2021.103548
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Title	Author, year	Doi / link
Incremental expenditures attributable to daily dispensation and witnessed ingestion for opioid agonist treatment in British Columbia: 2014–20	Nosyk 2023	10.1111/add.16160
Medication safety, privacy, and stigma: A qualitative study of pharmacy opioid agonist treatment disruptions and adaptations in the 2022 Northern Rivers floods, Australia	Caruana 2024	10.1016/j.ijdrr.2024.104244
Methadone for Opioid Use Disorder in the Fentanyl Era: Navigating Challenges and Evolving Strategies- a Narrative Review	Osagie 2025	10.1007/s40429-025-00655-6
Microdosing and standard-dosing take-home buprenorphine from the emergency department: A feasibility study	Moe 2020	10.1002/emp2.12289
Need for opioid agonist therapy among opioid users of open drug scenes	Zurhold 2024	10.62401/2531-4122-2024-58
Non-prescribed use of methadone and buprenorphine prior to opioid substitution treatment: lifetime prevalence, motives, and drug sources among people …	Johnson 2019	10.1186/s12954-019-0301-y
Opioid agonist treatment take-home doses (‘carries’): Are current guidelines resulting in low treatment coverage among high-risk populations in Canada and the USA?	Russell 2022	10.1186/s12954-022-00671-z
Patient Challenges in Utilization of Methadone to Treat Opioid Use Disorder and Perspectives on a Solution for Improved Security and Convenience in Take-home Dosing	Morse 2024	https://pmc.ncbi.nlm.nih.gov/articles/PMC11709438/
Patient perspectives on community pharmacy administered and dispensing of methadone treatment for opioid use disorder: a qualitative study in the U.S.	Wu 2023	10.1186/s13722-023-00399-6
Patterns of use and adverse events reported among persons who regularly inject buprenorphine: a systematic review	Bozinoff 2022	10.1186/s12954-022-00695-5
Policy and Practice of Opioid Agonist Treatment (OAT) in 23 Countries	Calvey 2025	10.1097/ADM.0000000000001519
Prevalence of diversion and injection of methadone and buprenorphine among clients receiving opioid treatment at community pharmacies in New South Wales …	Winstock 2008	doi: 10.1016/j.drugpo.2007.03.002
Provider experiences with relaxing restrictions on take-home medications for opioid use disorder during the COVID-19 pandemic: A qualitative systematic review	Adams 2023	10.1016/j.drugpo.2023.104058

Title	Author, year	Doi / link
Regaining control: the patient experience of supervised compared with unsupervised consumption in opiate substitution treatment	Notley 2014	10.1111/dar.12079
Simple, Rapid Spectrophotometric Assay of Dispensed Methadone for Diversion Control	Brooklyn 2022	10.1097/ADM.0000000000000990
Supervised Dosing With a Long-Acting Opioid Medication in the Management of Opioid Dependence	Dover 2020	Doi: 10.1097/NUR.0000000000000552
Supervised on-site dosing in injectable opioid agonist treatment-considering the patient perspective. Findings from a cross-sectional interview study in two German cities	Friedmann 2023	10.1186/s12954-023-00896-6
Uncommon and preventable: Perceptions of diversion of medication for opioid use disorder in jail	Evans 2022	10.1016/j.jsat.2022.108746
Usability and feasibility of a take-home methadone web-application for opioid treatment program patients: A Small Business Innovation Research mixed methods study	Giles 2024	10.1016/j.josat.2023.209181
Valuing methadone takeaway doses: the contribution of service-user perspectives to policy and practice	Treloar 2007	10.1080/09687630600997527
Workload, Usability, and Engagement with a Mobile App Supporting Video Observation of Methadone Take-Home Dosing: Usability Study	Idrisov 2023	10.2196/42654
“Sign Me Up”: a qualitative study of video observed therapy (VOT) for patients receiving expedited methadone take-homes during the COVID-19 pandemic	Darnton 2023	10.1186/s13722-023-00372-3
Early innovations in opioid use disorder treatment and harm reduction during the COVID-19 pandemic: a scoping review	Krawczyk 2021	10.1186/s13722-021-00275-1
Technology-assisted methadone take-home dosing for dispensing methadone to persons with opioid use disorder during the Covid-19 pandemic	Dunn 2021	https://scholar.google.com/scholar?cites=14355572411514126061&as_sdt=2005&sciodt=0,5&hl=en
Video directly observed therapy intervention using a mobile health application among opioid use disorder patients receiving office-based buprenorphine treatment: protocol for a pilot randomized controlled trial	Schramm 2020	https://dx.doi.org/10.1186/s13722-020-00203-9

Appendix 7—Data extraction table: Australian guidelines

Jurisdiction	Medication	Clinical setting(s) and indication	Patient characteristics	Initiation dose	Maintenance dose	Max dose	Takeaway dose setting and requirements	Requirements for supportive treatment	Prescriber/ patient limitations	Frequency of access
Queensland	Methadone	QOTP settings, including pharmacies and clinics	People with opioid dependence	Usually start 20–30 mg; max 40 mg in first week; dose should not increase by more than 5 mg in a day or 20 mg in a week; dose adjustments generally 5–10 mg at a time with 3 days in between	60–100 mg / day usual range, (standard upper limit of 100 mg / day); second opinion above 100 mg, ECG if > 150 mg / day	Standard upper dose limit of 100 mg, second opinion to go higher, ECG recommended above 150 mg / day (and considered above 100 mg / day)	Supervised first 3 months; takeaway only after risk assessment (not defined). Unsupervised doses should be diluted to 200 ml unless prescriber states otherwise. Higher risk patients may have 0-4 unsupervised doses a week; lower risk patients, max of 7 at a time	Psychosocial support encouraged	QOTP authorisation required, with levels of accreditation and temporary alternative prescribers (with no training) possible	Daily initially
Queensland	Sublingual buprenorphine (usually buprenorphine-naloxone)	QOTP settings, including pharmacies and clinics	People with opioid dependence	Traditional induction: 4–8 mg day 1; titrate in 2–4 mg steps; max 12–16 mg on day 1. Low-dose induction: commence 0.4 mg on day 1, increasing	Commonly 12–24 mg / day, but between 2 and 32 mg / day may be used	Up to 32 mg / day	Supervised initially; takeaway may be approved after stability / risk assessment (process not defined) up to monthly dispensing for lower risk, and 1-7 supervised doses a week for higher risk	Psychosocial support encouraged	QOTP authorisation required, with levels of accreditation and temporary alternative prescribers (with no	Daily initially, with un-supervised dosing depending on risk status

Jurisdiction	Medication	Clinical setting(s) and indication	Patient characteristics	Initiation dose	Maintenance dose	Max dose	Takeaway dose setting and requirements	Requirements for supportive treatment	Prescriber/ patient limitations	Frequency of access
				gradually while tapering other opioid					training) possible	
Queensland	Buprenor-phine LAIB (Buvidal®, Sublocade®)	Must be administered in clinic or pharmacy by healthcare professional	People with opioid dependence	Buvidal®: weekly 8–32 mg or 7 days of sublingual recommended prior to monthly injections	Buvidal® weekly / monthly; Sublocade® 100 mg monthly (after first two injections of 300 mg, or maintain 300 mg if needed)	Buvidal®: 160 mg monthly; Sublocade®: 300 mg monthly	Not applicable (clinic-administered only)	Psychosocial support encouraged	QOTP authorisation required, with levels of accreditation and temporary alternative prescribers (with no training) possible	Weekly or monthly depending on product
South Australia	Sublingual buprenorphine-naloxone	Un-supervised dosing	Stability assessed using risk assessment tool				Assessment of risk using a 2020 risk-assessment tool. High risk—only in exceptional circumstances; moderate risk up to 4 TA / week; low risk up to 28 days unsupervised			
South Australia	Methadone	Un-supervised dosing	Stability assessed using risk assessment tool				Assessment of risk using a 2020 risk-assessment tool. High risk—only in exceptional circumstances; moderate risk up to 2			

Jurisdiction	Medication	Clinical setting(s) and indication	Patient characteristics	Initiation dose	Maintenance dose	Max dose	Takeaway dose setting and requirements	Requirements for supportive treatment	Prescriber/ patient limitations	Frequency of access
							TA / week (consider if non-consecutive); low risk up to 4 TA / week			

Appendix 8—Data extraction tables: International guidelines

Country, medication	Clinical setting(s) and indication	Patient characteristics	Initiation dose	Maintenance dose	Max dose	Takeaway dose setting and requirements	Requirements for supportive treatment	Prescriber / patient limitations	Supervision of dosing
UK, methadone (oral)	Community pharmacies, GPs, drug treatment clinics	Adults with opioid dependence; caution in low / uncertain tolerance, comorbidities, sedative / alcohol use, mobility issues	Not specified in this guidance (referenced Orange Book)	Therapeutic range 60–120 mg / day	Typically ≤ 120 mg / day	Daily supervised dosing initially; takeaways only after stability and risk assessment	OST should be part of a support program; regular reviews and drug testing	Safe transfer required across settings; individualised supervision	Daily supervised at initiation; less frequent after stability
UK, buprenorphine (sublingual)	Community pharmacies, GPs, drug treatment clinics	Adults with opioid dependence; preferred if safety risk higher (overdose, comorbidities, alcohol l/ benzo use)	Usually 4–8 mg on day 1; can be lower (< 4 mg) or higher (> 8 mg) depending on case; may add 8 mg on day 2	8–16 mg / day; up to 32 mg / day	32 mg / day	May allow takeaways from start (up to 7 days) if safe; risk assessment required; lockable storage advised	OST part of support program; regular monitoring	Can be prescribed unsupervised at initiation in some cases; transfers must be managed safely	Daily at initiation; can reduce quickly to weekly in appropriate cases

Country, medication	Clinical setting(s) and indication	Patient characteristics	Initiation dose	Maintenance dose	Max dose	Takeaway dose setting and requirements	Requirements for supportive treatment	Prescriber / patient limitations	Supervision of dosing
USA, methadone	Opioid Treatment Programs (OTPs)	Adults with OUD; caution with low tolerance, sedative use, arrythmias	First dose ≤ 30 mg; total on day 1 ≤40 mg	Usual effective 60–120 mg / day	No federal maximum ; generally, not above 120 mg unless justified	Take-homes strictly phased: 1 / wk first 14 days; 2 / wk after 90 days; up to 1 month after 2 yrs' stability. Updated ruling (2024) for methadone to "allow up to 7 days of take-home doses during the first 14 days of treatment, up to 14 take-home doses from 15 days of treatment, and up to 28 take-home doses from 31 days in treatment. The requirement that OTPs maintain procedures to protect take-homes from theft and diversion is finalised, as well as patient education on safe transport and storage of take-home doses, including documentation of the provision of this education in the	Counselling required in OTPs	Methadone can only be dispensed via OTPs; strict monitoring	Daily observed initially

Country, medication	Clinical setting(s) and indication	Patient characteristics	Initiation dose	Maintenance dose	Max dose	Takeaway dose setting and requirements	Requirements for supportive treatment	Prescriber / patient limitations	Supervision of dosing
						patient's clinical record". https://www.federalregister.gov/documents/2024/02/02/2024-01693/medications-for-the-treatment-of-opioid-use-disorder			
USA, buprenorphine (sublingual)	Office-based waivered prescribers, community health centres, OTPs	Adults with OUD	First dose 2–4 mg; titrate to 8 mg day 1, 16 mg day 2 (Note ASAM guidelines report 2–4 mg, once objective withdrawal observed), increased in increments of 2–8 mg)	4–24 mg / day	FDA max 24 mg / day	May be prescribed for up to 30 days; early in treatment, prescribers must see patient weekly, then reducing to every 2 weeks, then monthly or less	Psychosocial support encouraged but not mandated	Requires DATA waiver (at time of TIP); pharmacy dispensing allowed	Frequent visits at initiation; can extend
USA, buprenorphine long-acting-injection (Sublocade®)	Given in clinic by healthcare professional	Adults with OUD stabilised on transmucosal buprenorphine ≥7 days	Start with 300 mg after stabilisation, after 7 days transmucosal buprenorphine (8-24 mg)	300 mg monthly × 2 months → 100 mg monthly (can remain on 300 mg)	300 mg / month	Not applicable (administered in clinic)	Psychosocial support required in OTPs; encouraged in office-based care	Must be administered by trained provider; risk evaluation and mitigation strategy	Monthly injection

Country, medication	Clinical setting(s) and indication	Patient characteristics	Initiation dose	Maintenance dose	Max dose	Takeaway dose setting and requirements	Requirements for supportive treatment	Prescriber / patient limitations	Supervision of dosing
								(REMS) required	
USA, buprenorphine long-acting-injection (BRIXADI)	Must be administered by a healthcare professional	Moderate to severe OUD in patients who have initiated treatment with a single dose of transmucosal buprenorphine or who are already being treated with buprenorphine	16 mg (weekly)	24 mg SC weekly; range: 8–32 mg or 96 mg SC monthly; range 64–128 mg	Maximum BRIXADI (weekly) dose being 32 mg or 128 mg per month of BRIXADI (per product information)	Not applicable (administered in clinic)	Psychosocial support required in OTPs; encouraged in office-based care	BRIXADI is subject to a Risk Evaluation and Management Strategy (REMS)	Weekly or monthly
Canada, methadone (oral)	Setting not specified; considered first line for opioid dependence (noting higher risk of mortality in first month)	Guidelines specific to adults (≥ 18) with OUD; guideline also reviews evidence for pregnant persons (no formal recommendation)	Not covered in 2024; CAMH guidelines recommend 5−30 mg, increasing by 5–15 mg every 3–5 days, with extreme caution if increasing by more than 10 mg at a time. Depending on tolerance	Not covered in 2024 (dosing schedules out of scope); 2018, most provinces have 60–120 mg, some up to 150 mg	Not covered in 2024; in 2018, 120–150 mg depending on province	Not covered (take-home doses out of scope)	Psychosocial interventions may be offered as adjuncts to improve retention; should not be mandatory. Harm reduction strategies should be offered	In Canada, exemptions to prescribe methadone have not been required since 2018 (per Health Canada website; https://www.canada.ca/en/health-canada/services/health-	Not specified in 2024

Country, medication	Clinical setting(s) and indication	Patient characteristics	Initiation dose	Maintenance dose	Max dose	Takeaway dose setting and requirements	Requirements for supportive treatment	Prescriber / patient limitations	Supervision of dosing
			(induction protocols and dosing schedules are out of scope—refers reader to provincial guidelines)					concerns/controlled-substances-precursor-chemicals/exemptions/methadone-program.html)	
Canada, buprenorphine (sublingual, incl. buprenorphine-naloxone)	Setting not specified; considered first line for opioid dependence (noting higher risk of treatment cessation in first month, but superior safety profile)	Guidelines specific to adults (≥ 18) with OUD; guideline also reviews evidence for pregnant persons (no formal recommendation)	Not covered in 2024; 2018 CAMH guidelines 2–4 mg (up to 6 mg). Reassess in 1–3 hours; consider prescribing additional dose up to max. 8 mg total on day 1	Not covered in 2024 (dosing schedules out of scope); in 2018, avg. 8–12 mg / day, max. 24 mg / day	24–32 mg	Not covered in 2024. In 2018, varies by province, often supervising for first 2 months, then 1–2 weeks TAs at a time, some states increase (e.g. one additional TA per 1–3 months)	Psychosocial interventions may be offered as adjuncts to improve retention; should not be mandatory. Harm reduction strategies should be offered	There are no special prescribing requirements for buprenorphine / naloxone in Canada	Not specified
Canada, slow-release oral morphine (SROM)	Setting not specified; second-line treatment behind methadone and bupren-orphine	Adults (≥ 18) with OUD; off-label for OUD in Canada	For patients using opioids other than methadone (e.g. heroin), prescribe 30–60 mg on day 1; noting people who	The average dose range is 200–800 mg / day (60–1200 mg / day in published literature)	Not covered	Prescribe take-home doses only in exceptional circumstances, where patients show high clinical stability, or when daily witnessed dosing is a barrier	Psychosocial / harm reduction as above	Second-line treatment; off-label; recommend experienced clinicians, close monitoring; daily	Not specified

Country, medication	Clinical setting(s) and indication	Patient characteristics	Initiation dose	Maintenance dose	Max dose	Takeaway dose setting and requirements	Requirements for supportive treatment	Prescriber / patient limitations	Supervision of dosing
			use fentanyl may need higher doses such as 100–200 mg. When switching from methadone to SROM, prescribe a methadone-to-SROM dose ratio of 1:4			to treatment. Consider graduated take-home dosing on a case-by-case basis. Follow up to prevent misuse or diversion. Before prescribing, conduct a comprehensive risk assessment and consult a specialist		witnessed doses and precautions initially emphasised	
Canada, injectable OAT (iOAT; e.g. hydromor-phone, diacetyl-morphine)	Clinic or pharmacy for supervised dosing; third line treatment, caution in use in people under 25 years old	Patients with severe OUD who inject opioids and have continued to experience significant health and / or social consequences related to their OUD despite past experience or attempts with appropriately dosed oral OAT, must be able to attend clinic / pharmacy up to three times daily, must be able to self-administer	60–120 mg hydromorphone on day 1 in split dosing with varying protocols depending on whether 2 or 3 times a day administration used; 120–240 mg diacetylmorphine on day 1, with varying protocols for 2 and 3 times a day dosing used	Typically, with oral OAT backbone	500 mg daily of hydromorphone (max 200 mg per dose) or 1000 mg daily (max 400 mg / dose) of diacetyl-morphine	Typically provided supervised; without provisions for regular unsupervised dosing	Embedded wrap-around care is the preferred model for delivering iOAT; integrated with services at community health centres, harm reduction programs and supportive housing programs to reduce barriers to treatment and address a range of health and social needs	Diacetylmorphine had specific regulatory controls that restricted its administration to hospital settings; however, these were lifted in 2018. Specific limitations on hydromorphone were not found	Typically, up to 3 times a day in a supervised setting

Country, medication	Clinical setting(s) and indication	Patient characteristics	Initiation dose	Maintenance dose	Max dose	Takeaway dose setting and requirements	Requirements for supportive treatment	Prescriber / patient limitations	Supervision of dosing
Canada, extended-release buprenorphine (e.g. Sublocade®)	Excluded from scope of 2024 guideline	Excluded from scope of 2024 guideline and 2018 guideline	Excluded from scope	Excluded from scope	Excluded from scope	Excluded from scope	Excluded from scope	Excluded from scope	Excluded from scope

Note: Norwegian guidelines did not include data on prescriber / patient limitations or frequency of access

Medication	Clinical setting(s) and indication	Patient characteristics	Initiation dose	Maintenance dose	Max dose	Takeaway dose setting and requirements	Requirements for supportive treatment
Norway, buprenorphine (sublingual)	Specialist health services; opioid maintenance treatment clinics; pharmacies	Strong recommendation in guidelines that methadone and buprenorphine are first line, with levomethadone or SROM offered if insufficient response to these. The primary target patient group is patients who have become opioid	2 mg if irregular use / low tolerance, increasing 2 mg / day; otherwise, if regular opioid use, 4 mg+4 mg on day 1 (observe for 30 min), 8 mg day 2, 12 mg day 3, 16 mg day 5 (5 min observation from day 2 onwards)	16 mg if effect is sufficient, increased per prescriber judgement	24 mg considered a high dose, a switch to methadone should be considered if this dose is not effective	When using methadone and oral morphine, more frequent intake under supervision may be more appropriate than when using buprenorphine. Individual arrangements determined based on patient current drug use, need, risk for diversion	Guidelines contain strong recommendation for comprehensive and coordinated rehabilitation. In Norway, patients in OAT are offered support with housing, finances, education, work and family / social networks, along with access to multidisciplinary specialised treatment, detoxification when needed, and mental

		dependent after using opioids as a drug. The recommendations may also be useful for people who have developed opioid dependence through pain management. Guidelines suggest considering switching to buprenorphine from methadone if sexual side effects or fatigue are present as buprenorphine may be associated with higher serum testosterone levels and perceived sexual function than methadone. Buprenorphine is associated with less fatigue than methadone, while no difference has been found between buprenorphine and methadone in terms of attention					health care for co-occurring disorders, all in line with national clinical guidelines. Psychological treatment recommended with benzodiazepine dependence for patients in OAT. Patients in OAT who, after assessment with a doctor, wish to taper off their substitution medication, should be offered gradual and long-term tapering, with adapted psychosocial follow-up and rapid dose increases if necessary

		and sleep problems					
Norway, long-acting injectable buprenorphine	Depot buprenorphine administered by healthcare personnel in specialist health services	Buprenorphine depot injection may be suitable for patients who need infrequent attendance for dispensing and intake under supervision due to rehabilitation measures, education, work, family life, or other reasons, as well as for patients who, due to difficulties with frequent attendance, may be at risk of dropping out of treatment	2-4 mg sublingual, then 16 mg with up to 2 x 8 mg top-up as needed with 1 day interval			NA	As above
Norway, methadone (oral) (liquid or tablets)	Induction inpatient or outpatient. Dispensing point can be: pharmacy, municipal services, e.g. home nursing, outpatient teams, estate follow-up, centres for delivery and social work follow-up,	Adults with opioid dependence; high risk of overdose early in treatment	Inpatient 20 mg if sporadic use / low tolerance (increase 10 mg every 3 days), 30 mg if regular use & moderate to high tolerance (increase 10 mg every 2–3 days). Observe for at least 2 hours after dose for 1–2 days after increase. Observe for	60–120 mg	Notes doses above 120 mg associated with increased risk of death, but may sometimes be required (no maximum dose stated), 120 mg considered a high dose	[For all medicine types] Consider if children in household. When using methadone and oral morphine, more frequent intake under supervision may be appropriate than when using buprenorphine. Frequency of taking substitution medication under supervision.	As above

	general practitioner offices, outpatient clinics in specialist health services, e.g. LAR outpatient clinic, DPS, outpatient follow-up from health and social care personnel in interdisciplinary specialised treatment (TSB)		intoxication after dose, reduce as needed			During escalation and the first 4–6 weeks on a maintenance dose, the substitution medication is taken under the supervision of a healthcare professional 5–7 days per week. After the first 4–6 weeks on the maintenance dose, the substitution drug is taken under supervision: 5–7 days per week in the case of extensive and addictive use of drugs, when the use has a risky effect on the patient. For example, in the case of high doses of benzodiazepines such as clonazepam or alprazolam, alcohol or stimulant drugs (amphetamine, cocaine). 2–4 days / week in case of addictive, but stable and low-grade use of drugs, when the use produces few risky effects. For example, in the case of stable use of low-to-moderate doses of benzodiazepines such as oxazepam or diazepam, or cannabis. 1–3 days per week when treated with benzodiazepines, without harmful and addictive use of drugs for 1 year. Then 2–4 days / month	
Norway, levo-methadone (oral)	Specialist health services; opioid maintenance treatment clinics; pharmacies	Strong recommendation in guidelines that methadone and buprenorphine are first line, with levomethadone or SROM offered if insufficient response to these	Levomethadone is the active enantiomer (form) of methadone and is registered as a LAR drug in Norway. The equipotent dose of levomethadone is half the dose of racemic methadone (e.g. 50 mg levomethadone is equivalent to 100 mg racemic methadone). Initiation doses are half of methadone initiation doses	30–60 mg			As above
Norway, slow-release oral morphine (SROM)	Inpatient, pharmacies, clinics, post-dose observation during induction recommended	Strong recommendation in guidelines that methadone and buprenorphine are first line, with levomethadone or	Usually initiated from methadone or buprenorphine; for those with regular opioid use prior, use 12-hour formulation 60 mg morning and night	600–800 mg for most patients	Ratio of 12-hour–24-hour can be 1:1 or 1:1.5 (e.g. a patient on 500 mg in 12-hour formulation may need 500–750 mg		As above

		SROM offered if insufficient response to these	day 1, increasing 20 mg / dose per day until 160 mg twice a day; doses above 320 mg after assessment; can switch to 24-hour formulation (i.e. 320 mg in a single dose) with 30 mg dose increases daily as needed based on clinical need (faster escalation possible in inpatient settings)		in 24-hour formulation); doses above 1200 mg not recommended	1 day per week for up to 1 year of absence from harmful and addictive use of drugs. 1–4 days / month with stable absence of harmful and addictive substance use for 1–5 years. Between 1 day / month and 1 day / year in the event of a stable absence of harmful and addictive use of drugs for 5 years or more. Discontinuation of regular intake under supervision may be considered. TAs not usually dispensed for more than 1 month's supply at a time. More frequent supervision considered if possibility of safe storage is reduced, or diversion occurs. In exceptional cases of long-acting morphine with an effect of up to 12 hours as a substitution drug (when tapering and switching between different substitution drugs), the drug is taken 2–3 times/day. Alternatively, the patient can take the morning dose under supervision 5–6 days per week, with correspondingly fewer supervised evening doses	