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Evaluation of Buvidal

Synthesis of findings

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Evaluation of Buvidal - Synthesis of findings

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Glossary

APB
Area Planning Board – a regional partnership body responsible for planning, commissioning and overseeing substance misuse services

Brixadi
The brand name of Buvidal in the US

Buprenorphine
A form of opioid substitution treatment (partial agonist)

BupSL
Sublingual (oral) buprenorphine

BupXR
Buprenorphine Extended Release - another name for long-acting injectable buprenorphine

Buvidal
A form of long-acting injectable buprenorphine

DBS
Disclosure and Barring Service

Espranor
A fast-dissolving wafer containing buprenorphine that is used as a form or opioid substitution treatment

HMPPS
His Majesty's Prison and Probation Service

LAIB
Long-Acting Injectable Buprenorphine

LM
Logic Model

Methadone
A form of opioid substitution treatment (full agonist)

NHS
National Health Service

NRC
National Research Committee

NRSI
Non-Randomised Studies of Interventions

OST
Opioid Substitution Treatment

PC
Project Consultants

PCC
Police and Crime Commissioners

R&D departments
Research and Development departments within local health boards

RCT
Randomised Control Trials

REC
Research Ethics Committee

SAIL
Secure Anonymised Information Linkage

SMAF
Substance Misuse Action Fund – funding provided by Welsh Government to Area Planning Boards to fund substance misuse services

Sublocade
A form of long-acting injectable buprenorphine

Subutex
A form of buprenorphine consumed orally

Third sector treatment providers
Charitable organisations that provide substance misuse treatment and support

ToC
Theory of Change

USW
University of South Wales

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1. Introduction

In March 2023, the Welsh Government commissioned a multi-disciplinary team of academics from three universities to undertake an evaluation of the rapid implementation of Buvidal across Wales. In this report we present a synthesis of the findings from this evaluation. In this introductory chapter we set the evaluation in context and provide a brief overview of the history of Buvidal in Wales. We also provide information about the evaluation team and the aims and objectives of the evaluation. The chapter ends with a summary of the contents of this report.

1.1. Background and context

People who become dependent on heroin or other illicit opioids often benefit from opioid substitution treatment (OST). OST medications broadly work by reducing or stopping withdrawal and cravings without producing the extreme highs that heroin and other illicit opioids can cause (Gov.uk, 2021). There is a strong evidence base for the effectiveness of OST. Research has shown that OST: is effective at suppressing heroin use; helps to retain people in treatment; is associated with better treatment outcomes; halves the risk of fatal overdose; helps to limit the spread of blood-borne viruses by reducing the rate of injecting; and is associated with decreases in drug-related acquisitive crime (Gov.uk, 2021).

The UK guidelines on clinical management of drug misuse and dependence are clear that OST has two core elements: pharmacological and psychosocial (The Orange Book, 2017). The pharmacological element involves substituting illicit opioids such as heroin with a prescribed alternative such as methadone or buprenorphine. The psychosocial element supports the substitution treatment by helping people to make positive changes to their lives (Gov.uk, 2021).

In the UK, two medications are recommended for use in the treatment of opioid dependence: methadone and buprenorphine. Methadone is a synthetic opioid agonist, which acts on the same receptors in the brain as heroin. While it occupies and activates these receptors, it does this slowly and produces some opioid effects such as emotional detachment and relaxation, but it does not produce the same high. Methadone is commonly prescribed as a liquid that is swallowed but it can be prescribed in tablet or daily injection.

Buprenorphine is a partial agonist that operates at the mu-opioid receptor and an antagonist at the kappa-opioid receptor. It acts on the same opioid receptors as heroin, but it activates them less strongly than full agonists such as methadone. It therefore has some of the same effects as methadone but less of a sedating effect. Buprenorphine is commonly prescribed as a sublingual tablet that dissolves under the tongue (Subutex) or as a freeze-dried wafer that disperses rapidly on the tongue (Espranor). One formulation of buprenorphine combines naloxone with buprenorphine (Suboxone). If taken as intended, this medication works the same way as normal buprenorphine. However, if the tablet is misused (e.g., by being crushed, injected or snorted), the naloxone (an opioid antagonist) will stop the buprenorphine working.

Risks associated with methadone and buprenorphine (e.g., diversion to others, non-medical use, and overdose risks), have led to a treatment model that is predicated on daily supervised consumption within services with take-home doses becoming available on the basis of a risk assessment and risk mitigation strategies (SMMGP, 2020). Not only is a daily dosing regimen

costly, research suggests that for some patients the inconvenience of attending a service daily is a barrier to engagement and retention is negatively affected (SMMG, 2020).

Buvidal is a depot formulation of buprenorphine designed for administration by subcutaneous injection (SMMG, 2020: 11). Formulated with the manufacturer's FluidCrystal injection depot technology, Buvidal is ready for use in pre-filled syringes that can be stored at room temperature. Buvidal is delivered in a similar manner to many vaccines (Scottish Government, 2020; Camurus, nd).

Buvidal injections are available in formulations that can be given weekly or monthly depending on the strength of the injection (BNF, 2024). Weekly Buvidal (8 mg, 16 mg, 24 mg, and 32 mg injections) has a terminal half-life[1] ranging from 3 to 5 days. Monthly Buvidal (64 mg, 96 mg, 128 mg, and 160 mg injections) has a terminal half-life ranging from 19 to 25 days.

The efficacy and safety of Buvidal in the treatment of opioid dependence has been established in clinical trials and Buvidal (known as Brixadi in the United States), was approved in the UK in November 2018 for the 'treatment of opioid dependence within a framework of medical, social and psychological support' (SMMG, 2020: 8).

1.2. Introduction of Buvidal in Wales

In England, Buvidal was reviewed and recommended for use by the National Institute for Health and Care Excellence in February 2019 (NICE, 2019). Following this approval, Buvidal was reviewed by the All Wales Medicines Strategy Group, and recommended for use in Wales in September 2019 (AWMSG, 2019). The All Wales Therapeutics and Toxicology Centre (AWTTC) reviewed this recommendation in November 2022 and as no new evidence was identified, the recommendation was transferred to AWMSG's static list of medicine recommendations (AWMSG, 2022).

Prior to the COVID-19 pandemic, Buvidal was already in use in some specialist and GP services in parts of England and Wales. In Wales, clinicians in Newport and Cardiff were piloting the medication and a small-scale evaluation was in its early stages (led by clinicians working for Kaleidoscope – a third sector treatment provider). However, as the pandemic unfolded and the need for social distancing gained momentum, alongside emerging positive evidence from Kaleidoscope's evaluation, a request was made to the Welsh Government for funding to make Buvidal available across the country. The Welsh Government subsequently allocated funding to support the rapid roll-out of Buvidal across Wales. The aim was to:

- provide safe and continuous management of dependency in a group that was thought to be at high risk of developing COVID-19, a group also thought to be at high risk of developing severe disease and at high risk of transmitting to others;
- proactively ensure that maintenance therapy is in place so that people dependent on heroin can self-isolate if they develop symptoms, if they have accommodation to do so, meaning they will not need to leave isolation for daily treatment or require daily delivery;
- achieve a rapid reduction in the need for daily contact with NHS front line staff and pharmacists to free them up for other tasks;

[1] "Half-life in the context of medical science typically refers to the elimination half-life. The definition of elimination half-life is the length of time required for the concentration of a particular substance (typically a drug) to decrease to half of its starting dose in the body." (Hallare and Gerriets, 2023).

- reduce the risk of transmission of COVID-19 to other vulnerable patients in clinics and at community pharmacies;
- free capacity in specialist supervised consumption services, to support the most complex patients, including supporting the homeless sector in moving rough sleepers off the streets into accommodation and support; and
- to ease pressure associated with the potential early release of prisoners.

Prior to the pandemic, the Welsh Government's Substance Misuse Strategy (or 'Delivery Plan') made no reference to long-acting buprenorphine (Welsh Government, 2019). However, in early 2021, the plan was amended to ensure it reflected 'the work that has been, and will be, undertaken as a result of the pandemic' (Welsh Government, 2021, p.1). The revised plan highlighted the work being undertaken to support the rapid introduction of Buvidal across Wales to ease pressure across prescribing services. Importantly, it included a commitment to evaluate the impact of Buvidal.

Since that time, Buvidal has been implemented across Wales and the Welsh Government has ringfenced £3m of its annual budget, to continue Buvidal alongside a longer-term full evaluation (Welsh Government, 2022). The adoption of Buvidal is now significantly higher in Wales (33%[2]) than in England (2.8%) given the Welsh Government's decision to support costs centrally (Hansard, March 2025). It is also higher than in Spain and France (where less than 2% of patients are prescribed Buvidal) but lower than in Finland where 60-65% of patients on OST are prescribed Buvidal (Rolland et al., 2025).

1.3. Evaluation team

The evaluation team comprised a group of researchers who together brought specialist knowledge and expertise in a range of areas relevant to this evaluation, including opioid substitute treatment, primary care, clinical trials, evaluation research, economic evaluation, theory of change and logic model development, systematic review, qualitative research with stakeholders and vulnerable groups, safeguarding, and research ethics. The team comprised staff from across three academic institutions (University of South Wales, University of Hertfordshire and Wrexham University) and included criminologists, psychologists, a social worker, a consultant addictions psychiatrist, a medically trained researcher, and a statistician.

1.4. Evaluation aims

The aim of the evaluation was to provide 'timely, robust information on the implementation and indicative outcomes of the introduction of Buvidal across Wales and particularly on the wider service impacts and potential future adaptations required as a result of this new treatment'. The evaluation also aimed to provide 'some assessment of the value for money elements of this treatment, including wider savings'. Put simply, the aim was to conduct a process, impact and economic evaluation of Buvidal.

1.5. Evaluation plan

The evaluation was originally designed as a three-stage process that would be delivered over a 2-year study period. In practice, however, the stages overlapped, and the individual work

[2] This figure is based on our analysis of data from the SAIL databank (see Chapter 6 for further details).

packages were delivered concurrently. This shift was necessitated by the study being defined as 'research' rather than a 'service evaluation' by the health boards, which meant that approval was needed from an NHS Research Ethics Committee, as well as confirmation of capacity and capability from each health board, before data collection involving NHS staff or patients could begin (NHS Health Research Authority, 2022).

Rather than delay progress while awaiting these approvals, work was initiated on those strands of the evaluation that did not require ethical approval (i.e., the systematic review) and, subsequently, on those that could proceed solely with ethical approval from the University of South Wales (USW) (i.e., data collection involving non-NHS/HMPPS staff and patients). Table 1 provides further information about the evaluation timeline.

Table 1 Evaluation timeline

Work package	Start	End	Notes
Systematic review of the literature	Oct 2023	Jun 2025	First search was run in Dec 2023 and updated in May 2025
Interviews with stakeholders	May 2024	Feb 2025	Interviews with non-NHS/HMPPS staff began in May 2024. Interviews with NHS/HMPPS staff began in Oct 2024.
Survey with stakeholders	Nov 2023	Feb 2025	Survey was opened to non-NHS/HMPPS stakeholders in Nov 2023 and to NHS/HMPPS stakeholders in Aug 2024
Focus groups with patients	Jul 2024	Feb 2025	Focus groups with third sector patients began in Jul 2024 and with NHS/HMPPS patients in Nov 2024
Quarterly monitoring returns	Nov 2023	Dec 2023	Preliminary analyses identified gaps and inconsistencies in the 'tracker' submissions. Further analyses were not undertaken given our access to linked data in the SAIL databank[3].
Case file review	Nov 2024	Dec 2024	Preliminary analyses of a sample of files showed that they did not contain sufficiently rigorous data with which to explore novel outcomes. Further analyses were therefore not undertaken.
Theory of Change and Logic Model development	Jan 2024	Jun 2025	Four face-to-face workshops were held throughout Nov 2024, and one online workshop was held in Jan 2025
SAIL data analysis	Oct 2024	Incomplete due to data sharing agreement delays	Data were provisioned to us by SAIL in Oct 2024. MOJ data have not yet been provisioned.

1.6 Structure of report

In addition to this introductory chapter, this report includes eight further chapters. Chapter 2 provides an overview of the methodology that underpins the evaluation and identifies the main strengths and limitations of the project. Chapter 3 summarises the findings from a systematic

[3] SAIL (Secure Anonymised Information Linkage) Databank is a rich and trusted population databank that is ISO 27001 certified and UK Statistics Authority accredited. It provides researchers with secure, linkable and anonymised data.

review of the literature on the effectiveness of long-acting injectable buprenorphine. Chapters 4 and 5 draw on data collected from stakeholders and patients and summarise, respectively, findings from the process and impact evaluations. Chapter 6 summarises findings from our comparison of healthcare service usage and associated costs among patients on different forms of OST using data from the SAIL databank. Chapter 7 presents a theory of change and logic model for Buvidal developed collaboratively with input from stakeholders in a series of workshops across Wales. Chapter 8 focuses on the future of Buvidal in Wales drawing on the perspectives of stakeholders and patients. The final chapter discusses the findings in light of the literature reviewed in Chapter 3 and sets out our recommendations for the future delivery and development of Buvidal in Wales. More detailed information about each strand of the evaluation can be found in the series of supplementary reports that will be published alongside this synthesis report.

2. Methodology

In this chapter, we provide readers with summary information about the evaluation aims, the methods used to achieve those aims, the strengths of the evaluation and the limitations that need to be borne in mind when drawing conclusions from the findings presented. More detailed information about the methods used in this evaluation will be presented in full in a separate Methods report.

2.1. Evaluation aims

The evaluation was complex, multi-faceted, and included both backward and forward-looking components to serve three aims:

1. to assess how the programme had been set up and how it was being operated (backward looking).
2. to elucidate the theory of change for Buvidal and develop the logic model underpinning the treatment, considering the differences between Buvidal and other OST and what a 'new' service could look like (forward looking).
3. to provide an indication of its overall effectiveness and an economic evaluation (including any differences between outcomes for those on Buvidal and other OST medications) (backward looking).

Based on a realist methodology, which assumes that the same intervention will not work everywhere or for everyone, the evaluation sought to assess not only whether Buvidal was effective, but also how, why, for whom and under what circumstances (Mercer and Lacey, 2021). In practice, the evaluation comprised multiple interconnected strands, including: a systematic review of existing evidence on the effectiveness of long-acting injectable buprenorphine; the collection of primary qualitative (and some quantitative) data from professional stakeholders and patients using mixed methods; and secondary analyses of quantitative data from the SAIL databank. Table 2 links each strand of work to the relevant research aim(s) and provides information about the target population, sampling approach, and both the expected and achieved sample sizes.

2.1. Analysis of primary data

Qualitative data from interviews and focus groups were analysed using NVivo software. Three members of the research team (KH, MB, JM) were involved in the analysis, which followed a multi-stage process. Initially, a coding framework was developed, informed by relevant literature as well as the team's experiences in conducting the interviews and focus groups. This preliminary coding structure was then tested on an interview transcript, with each team member independently coding the text. Their codes were subsequently compared and discussed to ensure consistency and clarity. Based on this collaborative review, the coding framework was revised and further tested on a focus group transcript. After final refinements, the framework was applied to the remaining interview and focus group transcripts. These were divided among the three analysts and coded separately in individual NVivo projects. Once coding was complete, the projects were merged into a single master NVivo file, which served as the foundation for a detailed thematic analysis.

Quantitative survey data were downloaded from Jisc Online Surveys and analysed in SPSS. The analysis focused on descriptive statistics, with frequency distributions used to summarise participants' responses. A limited number of cross-tabulations were also conducted to examine associations between key demographic and response variables.

Table 2.1 Overview of methodology

Research aims	Method	Population	Sampling approach	Expected sample size	Achieved sample size
2, 3	Systematic review	Academic sources	Systematic	n/a	11 – quantitative papers 19 – qualitative papers
1, 2, 3	Semi-structured interviews	Stakeholders involved in delivery of Buvidal	Purposive and snowballing	50	52
1, 2, 3	Online questionnaire survey	Stakeholders involved in delivery of Buvidal	Purposive and snowballing	100	114
1, 2, 3	Focus groups	Patients with experience of OST	Purposive and snowballing	7	7 (n=28)
2	Workshops	Stakeholders involved in delivery of Buvidal	Purposive and snowballing	4	5 (n=17)
3	SAIL analysis	Patients receiving methadone, oral buprenorphine and Buvidal from 01/04/2020	Whole population	n/a	5,030 patients, 9,010 journeys, 10,348 records

Notes: While targets were set for the number of focus groups and workshops, no specific targets were set for the number of participants per group.

2.2. Ethical considerations

2.2.1. Approval

Ethical approval for the evaluation was obtained from USW, the NHS (Wales REC 4 – IRAS Project ID: 331415), and the HMPPS National Research Committee (Ref: 2024-1109). Once Research Ethics Committee (REC) approval had been granted, confirmation of capacity and capability was obtained from each health board research and development (R&D) department. Approval for access to the SAIL databank was obtained from the independent Information Governance Review Panel (IGRP) (ID: 1716). The IGRP contains independent members from the National Research Ethics Committee (NREC) and the British Medical Association. The

IRGP confirmed that the evaluation is useful, not a service evaluation, and that we would not break anonymisation standards.

This was a complex evaluation comprising multiple strands of work, each requiring careful attention and ethical scrutiny. All components of the evaluation involving interaction with participants adhered to core ethical principles, including obtaining informed consent from all participants prior to their involvement; ensuring the safety and well-being of both participants and researchers; respecting participants' privacy; and maintaining transparency about the nature of participation, with a clear commitment to avoiding deception.

2.2.2. Process of obtaining approval

Obtaining ethical approval for the evaluation took longer than anticipated. As the evaluation involved staff and patients from NHS, HMPPS and third sector organisations, ethical approvals, and permission to collect data were required from a range of stakeholders necessitating a large volume of email communications and meetings. While we (i.e. the evaluation team) were aware from the outset that HMPPS approval would be required given the involvement of criminal justice staff and patients, we had anticipated that as a 'service evaluation', NHS approval may not be needed.

Early engagement with HCRW and health board R&D departments took place in July and August 2023. The health board R&D departments assessed the evaluation as 'research', which meant that the project required formal review (via IRAS) by a national Research Ethics Committee (REC) and subsequently confirmation of capacity and capability by each participating health board before any kind of data collection involving NHS staff or patients could begin. USW ethical approval was also necessary (and mandatory prior to submitting the IRAS application).

To ensure data collection could begin as swiftly as possible, we proceeded first with low-risk applications to USW for the stakeholder online survey and interviews with non-NHS/HMPPS staff. These were submitted in November 2023 and approved in December 2023. This was then followed by high-risk applications to USW for focus groups with non-NHS/HMPPS patients submitted in December 2023 and approved in February 2024. Note the USW high-risk panel sits once per month.

The IRAS paperwork was completed for NHS/HMPPS staff and patients and after internal approval by USW ethics committee, this was submitted in March 2024, and we attended the REC panel in June 2024. It is important to note that there were four strands of work each involving a detailed protocol, information sheets, consent forms, data collection tools (survey, interviews, focus groups, workshops). In line with IRAS requirements, the protocols were reviewed by two external reviewers who were independent of the evaluation prior to submission to IRAS. The reviewers were invited by the evaluation team to review the paperwork and their feedback was addressed prior to submission.

REC approval was granted on 25 July 2024. Final sign off from Wales REC 4 was issued on 14 August 2024 with a formal letter advising us that it had been approved, but that we could not begin collecting data until the health boards had confirmed they had capacity and capability to support the project. We liaised with HCRW who sent out an email to all R&D departments on 6 September 2024 asking them for their support. Powys opted out at an early

point on the basis that they did not have any statutory OST services. Our first capacity and capability approval was obtained mid-October 2024, with the final approval being received in December 2024.

USW approval was then needed for workshops with non-NHS/HMPPS staff (on the back of the REC approval) and secondary data analyses (SAIL data and case file review[4]) and these were approved on 14 October 2024. HMPPS approval was granted on 11 July 2024. In September 2024, the Prison Group Director for Wales gave their support to the project subject to each prison Governor agreeing. Support from the Probation lead was also secured in September 2024. Approvals from participating prisons were in place by November 2024.

2.3. Strengths and limitations of the evaluation

The evaluation demonstrated strength in several areas.

It was conducted by a large, multi-disciplinary team of experienced researchers and guided by a team of project consultants with lived experience of substance use and/or supporting people with substance use problems.

Unlike many previous evaluations of injectable buprenorphine, this evaluation was funded by Welsh Government rather than by the medication's manufacturer. This helped to reduce the risk of bias and enhance the credibility of the findings.

The evaluation included an extensive and systematic review of the literature on the effectiveness of injectable buprenorphine. The review was distinctive in its exploration of a wide range of health and social outcomes. Not only did the review inform the design and conduct of the evaluation it also provided valuable context within which to review the findings.

The evaluation was national in scope (covering the whole of Wales) and based on a robust mixed-methods design. Qualitative data were collected from stakeholders working across a diverse range of fields through semi-structured interviews, an online survey and workshops, as well as from individuals with experience of receiving Buvidal through focus groups conducted in community and prison settings. This comprehensive design enabled triangulation of findings across multiple data sources, thereby enhancing the credibility, validity and robustness of the evaluation.

Quantitative data from the SAIL databank were used to compare patients on different forms of OST in terms of their healthcare usage and associated costs. The analysis presented is based on the largest known sample of patients on long-acting injectable buprenorphine globally.

Finally, this evaluation was distinctive in developing, for the first time, a detailed theory of change and logic model for Buvidal. This provides a valuable framework for helping to understand how and why Buvidal achieves its outcomes.

Despite its many strengths, the evaluation also has several limitations that should be borne in mind when reviewing the findings.

[4] A feasibility study involving scrutiny of a sample of case files from one Buvidal service, resulted in this strand of work being discontinued. The study demonstrated that there were insufficient data within the files to identify any additional outcomes, which was the primary purpose of the case file review.

The lengthy delays in securing necessary approvals from the NHS and the health boards has meant that some time has passed since the first interviews were conducted. It is possible that changes may have occurred in that time (e.g., in staffing, funding, and outcomes).

We were unable to access any stakeholders in one English prison and no clinical stakeholders in one Welsh prison, which meant that we were not able to explore fully the use (or not) of Buvidal in those locations.

While we reached out to a wide range of established stakeholder networks and gatekeepers, there may be bias in those identified and self-selection bias among those who engaged. This may mean the perspectives of stakeholders choosing to engage in the research are different to those who were unable or not interested.

A similar limitation applies to our focus group participants. While all participants had experience with different types of OST, most were on Buvidal at the time of the focus group discussions. This means that first-hand accounts from those who had either declined or dropped out of Buvidal treatment were not included.

There was limited attendance from stakeholders in one area at both the in-person theory of change (ToC) workshop and the online event that was specifically arranged to give stakeholders in this area another opportunity to contribute to the evaluation.

Our analyses of the SAIL data were thwarted by inaccurate and incomplete entries within the substance misuse database, problems which have also been reported by Public Health Wales (2025). This meant that a series of assumptions and principles had to be made with the input of professional opinions, which were then applied to 30% of all treatment records. The impact of this on the findings is not clear.

While the evaluation was pan-Wales and involved data collection across all seven health board areas, some areas had better representation within the evaluation than others.

2.4. Evaluation reports

In the series of supplementary evaluation reports that will be published alongside this one, we present detailed findings of our in-depth evaluation of the rapid roll-out and implementation of Buvidal in Wales. The reports draw extensively on the data collected from interviews with 52 stakeholders, survey responses from 114 stakeholders and discussions from seven focus groups involving 28 patients. While trying to balance the need for brevity (to suit a policy audience) with the need to provide evidence and further detail (to suit academic and practitioner audiences), we have limited our use of quotations as far as possible in those reports to one or two examples of each point.

In this report we summarise and synthesise findings from the series of evaluation reports and provide recommendations to help guide the future delivery of Buvidal in Wales.

3. Systematic review

- To assess the current state of knowledge on the effectiveness of Buvidal and other forms of long-acting injectable buprenorphine (LAIB), a systematic review of the literature was conducted.
- Eleven quantitative studies met the inclusion criteria and comprised three randomised controlled trials (RCTs), one pilot randomised comparative effectiveness trial and seven non-randomised studies of interventions (NRSIs). Methodological issues were noted in all included studies.
- Nineteen qualitative studies met the inclusion criteria, and our quality appraisal of these studies was largely positive.
- Most studies were funded by pharmaceutical companies involved in the production and distribution of LAIB.
- No difference between LAIB and other opioid substitution treatments (OST) were found in terms of deaths, though patients on LAIB appeared less likely to experience overdoses.
- Those treated with LAIB reported greater opioid abstinence than those treated with other forms of OST, although methodological weaknesses in the NRSIs limit confidence in these findings.
- Patients on LAIB reported greater improvements in mental health and quality of life, though some experienced difficulties in these areas and may require additional support.
- Among randomised studies, treatment retention was better in the LAIB group in the short term, although worse in the long-term. Qualitative evidence suggests this may be related to trial contexts removing the financial incentives to use and continue LAIB.
- Withdrawal and craving data were largely mixed, and the complexity of these outcomes was reflected in the qualitative data.
- Reincarceration was lower among those treated with LAIB, potentially due to reduced medication diversion and withdrawal-driven reoffending.
- Overall, more trends appeared to favour LAIB than other forms of treatment, although more high-quality research is necessary to confirm this

3.1. Introduction

One aim of this evaluation was to assess the current state of knowledge on the effectiveness of Buvidal and other long-acting forms of opioid substitution treatment. To achieve this, we conducted a systematic review of the research evidence, the findings of which are summarised here. Systematic review methodology allows for a rigorous consideration of existing published research through setting a priori prescribed inclusion criteria and search algorithms; conducting quality assessments and risk of bias analyses on included research studies; and synthesising strengths and significance of reported findings, including methodological rigour. The review comprises a separate output that details the registered review protocol, search terms, PRISMA flow chart, detailed discussion of findings, and additional information regarding study characteristics, risk of bias analyses and conflicts of interest.

3.2. Review question

Is long-acting injectable buprenorphine (LAIB) more effective than other forms of treatment for opioid use disorder in improving the health and social outcomes of adult (18+) patients?

3.3. Included studies

Eleven quantitative studies met the inclusion criteria and comprised three randomised controlled trials (RCTs), one pilot randomised comparative effectiveness trial and seven non-randomised studies of interventions (NRSIs). There were methodological issues noted in all included studies, with the randomised studies unsurprisingly presenting the strongest study designs. Weaknesses with these included the majority being open-label (unblinded) studies.

The NRSI papers presented additional problems, often related to the fact they were observational case-record review studies and not shortcomings on the part of the authors. An example of this is inconsistency in the reporting of treatment time frames, such as one study where the number of participants retained for 6-months or more was reported, but many service users had dropped out of treatment prematurely and so outcomes may not truly reflect a '6-months in treatment' timeline. We consider identified biases in all studies and their potential impact on confidence in reported outcomes in detail in the full report.

Nineteen qualitative studies met the inclusion criteria, employing a range of methodological approaches. Our quality appraisal of the extracted qualitative studies was largely positive, with all studies demonstrating congruity between their research methodology and their questions, data collection methods, analysis of data, and interpretation of results. All studies drew conclusions that were deemed to flow from their analysis and interpretation of data. Most findings achieved high levels of credibility, which means they were directly inferred from the data and supported by participant quotations.

Risk of bias assessments also revealed that the majority of both qualitative and quantitative studies were funded by pharmaceutical companies involved in the production or distribution of LAIB.

3.4. Outcomes reported

Where possible, outcomes were separated into long- and short-term outcomes, using 24-weeks as the cutoff point, though this was often not possible for the NRSIs due to their design. Quantitative findings are summarised in the effect direction plots (see Annex Figures 3.1-3.3) at the end of the chapter.

3.4.1. Death

Low incidence of deaths was reported across all studies that measured this outcome, six in total. The cause of one death was unknown, and all others were judged to be unrelated to the drugs of treatment in the studies. These findings suggest that deaths are unlikely to occur when clients are in any form of OST treatment, although some studies were unclear about how they recorded deaths.

3.4.2. Overdoses

Overdoses were also rarely reported in any group, particularly at the early stages of treatment. Slightly fewer incidents of overdose were noted in LAIB patients than those on daily treatments in studies with longer term follow up. This suggests that whilst overdose in treatment is unlikely, they are even less likely in LAIB treatment.

3.4.3. Treatment retention

Retention was conceptualised as retention on the initially prescribed OST and not including treatment switching. The findings were somewhat mixed, with the randomised studies favouring the LAIB group in the short term but reporting higher retention rates in the daily treatment group at week 24, suggesting any initial benefits of high retention for LAIB patients might dissipate over time. The NRSI studies for the most part reported good treatment adherence in LAIB and both methadone and daily buprenorphine comparator groups, although overall retention rates were higher in the LAIB groups, including in the longer term. Caution should be exercised with the NRSI findings, as one of these studies favouring LAIB relied on a relatively small sample.

The qualitative findings provide additional insights into retention. One long-term study found that individuals who remained in treatment up to the 12-months point reported sustained positive outcomes, which the researchers interpreted as a qualitatively different phase of recovery. Participants from some studies, particularly in Australia, identified the financial burden of daily medication as a key driver to both initiate and maintain LAIB treatment, as the cost is much lower. These authors conclude that this could be a significant influence on LAIB retention levels. The removal of this financial benefit of LAIB during trials (i.e., because daily medication costs are removed) may be an important factor to consider in the context of its poorer observed retention rates.

3.4.4. Abstinence

Abstinence outcomes were measured in numerous ways; abstinence from opioids was the primary measure, and studies also examined abstinence from stimulants, benzodiazepines and alcohol, and all substances combined, the latter being for the most part explored qualitatively.

Abstinence – opioids

All three RCTs reported that in the short term LAIB groups did better than daily dose groups. Two out of three of these trials found that this trend continued long term, suggesting that LAIB may offer superior opioid abstinence, especially in the short term, but that this effect may weaken over time. The NRSI studies also mostly favoured LAIB with only one out of five finding daily treatment to have better abstinence rates. Some caution is needed when interpreting the findings of the observational studies, however, for a range of issues including only reporting data for treatment completers, not accounting for treatment switching, and variability in how missing data were handled. Despite these caveats, the current evidence suggests that LAIB is generally associated with higher rates of abstinence from opioids than other OSTs. Qualitative data suggests this may partly be due to reduced peer contact.

Abstinence – Stimulants, Benzodiazepines, Alcohol.

Only one study (an RCT) provided abstinence data relating to stimulants, benzodiazepines and alcohol use. For stimulants and benzodiazepines, a trend favouring the LAIB group was reported, but the findings regarding alcohol were mixed. The LAIB patients reported drinking less frequently, but they consumed more than daily dose patients on actual drinking days. These are interesting differences between substances, albeit they come from a single study. Qualitative data suggests LAIB patients may begin to engage in more socially accepted substance use (i.e., alcohol) in the absence of their opioid use.

Abstinence – all illicit drug use

Three quantitative studies provided data on the impact of treatment on combined opiate/illicit drug use and included five comparisons in all. Three out of five of these found that LAIB groups did better than daily dose groups, although there are caveats for these findings relating to self-reported abstinence data. Some qualitative studies attempt to explore the complexities behind the quantitative abstinence findings. Whilst consistently highlighting LAIB's ability to promote opiate abstinence, there is considerable variation across individual patients. Reduced peer contact that accompanies monthly or weekly treatment was again cited as a factor in reducing incidence of illicit drug use.

Overall, the abstinence data suggest a trend for LAIB to be more effective than daily doses, but long-term high-quality evidence is currently fairly limited.

3.4.5. Withdrawal symptoms

The experience of withdrawal is often complex and can vary considerably between individuals. Two RCTs reported data on withdrawal symptoms, with one suggesting patients receiving LAIB may be less likely to experience withdrawal symptoms in the short-term. Long-term findings contradict this, with one study showing no differences and the other finding greater withdrawal symptoms in the LAIB group. Two NRSI studies also reported on withdrawal symptoms, and similarly provide a mixed picture, with one finding that LAIB patients fared better and the other showing no clear direction. However, both have methodological limitations in terms of samples used (i.e., small and unrepresentative) and handling of missing data.

The qualitative evidence provides nuanced insights into individual withdrawal experiences. With LAIB treatment, the evidence suggests that symptoms vary in intensity at different time points in the treatment cycle. These may be stronger at the start of treatment, especially during the titration process, and may persist until optimal dosage levels are achieved for that individual patient, after which point there may be little or no experience of symptoms. For some patients, experimenting with extending times between doses beyond recommended intervals has led to experiencing withdrawal symptoms. This seems to occur in the longer term when individuals have been exposed to LAIB treatment for 12 months or often longer.

3.4.6. Cravings

The evidence presented from the RCTs relating to craving control does not consistently favour either LAIB or daily dose OSTs, with the NRSI studies similarly presenting conflicting findings. Overall, it would appear cravings may initially be better controlled under LAIB treatment, but this difference may fade with time. The qualitative research provides important context to the

issue of craving and how many service users are very frightened of experiencing it, and the lengths they will go to avoid it. These findings suggest that reduction in opioid cravings is a key LAIB benefit for some individuals, even when missing scheduled doses. However, this is not a universal experience and given the absence of consistent trends, any conclusions around the impact of LAIB on craving remain tentative.

3.4.7. Mental health

Perhaps surprisingly, anxiety and depression were rarely reported as individual outcome measures by the included studies, with none reporting the former and only one the latter. Given the salience of mental health status to the review topic, we made the decision to group all mental health related outcomes together, thus the findings here should be considered with this as a caveat. These included measurements of depression, emotional dysregulation, and more general psychological distress and psychological health

Two RCTs presented long term data on the impact of treatment on mental health, both reporting trends favouring the LAIB group. One of these also found short-term benefits of LAIB treatment. A large NRSI study similarly found better mental health outcomes in LAIB patients, confirming the findings of the RCTs. The qualitative evidence further supports a positive effect on mental health for LAIB patients. Patients noted improved mood, stability and reduced anxiety, although the latter was often initially raised due to concerns about potential withdrawal symptoms with the new treatment. Some felt LAIB treatment eliminated certain daily stressors that they were used to experiencing, such as worries about medication access, pharmacy visits and other reminders of addiction status, and associated feelings of stigma. Taken together, these findings suggest LAIB may be more beneficial to mental health compared to daily treatments. However, there were also reports of increased anxiety for some individuals, which may be related to preexisting or re-emerging conditions, suggesting the need for caution in over-interpreting trends identified by a small number of studies, especially given the breadth and complexity of mental health issues. Moreover, LAIB was seen as potentially creating an opportunity for individuals to improve their mental health by offering mental clarity and presence, which other treatments did not, and allowing engagement with psychological therapy, perhaps due to this increase in mental clarity.

3.4.8. Quality of life

Both RCT and NRSI studies point to LAIB treatment leading to a better quality of life compared to daily OSTs. Individual accounts from the qualitative studies illustrate this finding through highlighting that LAIB had substantial positive impacts on their quality of life, particularly in terms of daily living, relationships, and personal freedom. The transition from daily dosing to monthly injections represented a fundamental shift in how patients structured their lives, freeing them from what was described by one as "liquid handcuffs”.

3.4.9. Criminal activity

Criminal activity was not measured in any of the included quantitative studies, but two provided data on reincarceration of former offender populations. Both found that oral buprenorphine patients were more likely to be returned to prison than those on Buvidal, but methodological limitations might affect validity with these findings. Qualitative findings suggest both direct and

indirect effects of LAIB treatment on criminal activity. Key examples of these included the elimination of medication diversion opportunities and withdrawal-driven reoffending.

3.4.10. Employment, education or training

One very small pilot study provided the only quantitative data on this outcome. They found three out of five patients were employed at baseline and the same number were employed at follow-up, indicating no changes to employment following LAIB initiation. Positive outcomes were presented in the qualitative data, many of which seem to result from the flexible nature of monthly dosing in fitting in with employment and other commitments. Being released from a daily treatment regime appears to facilitate broader aspirations in relation to education and training.

4. Process evaluation

- To assess the roll out, implementation and delivery of Buvidal in Wales, a process evaluation was conducted drawing on the perspectives of professional stakeholders and patients.
- The urgency of the COVID-19 pandemic created a unique opportunity to fast-track Buvidal's roll out across Wales. While this led to innovation and broad uptake it also meant bypassing usual checks and structures. As a result, services were set up unevenly, contributing to variability in delivery across areas.
- Initially hailed as a 'game changer' by stakeholders and patients, Buvidal quickly gained popularity. Over time, it has been recognised not as a cure-all, but as one element within a broader treatment framework.
- Stakeholders and patients increasingly stress the need for wraparound support, including psychological care, psychosocial interventions, and skilled staff to address the emotional clarity and challenges Buvidal can bring.
- Ring-fenced Welsh Government funding for Buvidal covers only the cost of the medication, leaving services to fund all other related expenses from already over-stretched budgets. Clinical regulations and licensing requirements further strain resources. Most areas have mitigated this using slippage from other budgets.
- The initial roll out was reactive with limited guidance available to services. Confidence has grown, but many services still operate in isolation, missing opportunities to share best practice. Training gaps remain around clinical administration, mental health impacts, and patient engagement.

4.1. Introduction

A key aim of the evaluation was to provide timely, robust information on the implementation of Buvidal across Wales and to assess how the programme has been set up and how it has been operating. To achieve this aim, we conducted a process evaluation that drew on the perspectives and experiences of those involved in commissioning and delivering Buvidal treatment (i.e., stakeholders) as well as those involved in receiving the treatment (i.e., patients). The stakeholders were a diverse group of professionals working in a variety of occupations across Wales, including nurses, peer workers, support workers, social workers, psychologists, GPs, service managers, policy makers and consultant addictions psychiatrists.

Detailed findings from the process evaluation comprise a separate output. Here we present a summary of that report, focusing on 10 themes relating to the processes and practices underpinning Buvidal delivery in Wales (see Annex Figure 4.1 for an overview). These themes relate to knowledge and acceptability; availability of Buvidal; funding and commissioning; administering Buvidal; initiation and maintenance; additional support; eligibility criteria; guidance and training; licence requirements; and exiting treatment.

4.2. Knowledge and acceptability

By the start of the COVID-19 pandemic, awareness of Buvidal was widespread among stakeholders. Some stakeholders had learned about Buvidal through attendance at a seminar

in Birmingham in 2019, while others had been approached directly by sales representatives of the manufacturer. Others first learned about Buvidal through an email from the Welsh Government to Area Planning Board (APB) Chairs and substance misuse leads in April 2020, which announced that funding for Buvidal would be forthcoming.

Initial optimism surrounding Buvidal was strong with the term ‘game changer’ becoming its strapline. However, this initial enthusiasm was tempered by concern it could leave some patients vulnerable to relapse given the clarity of mind and resurfacing of emotions reported by many patients. At that time, the focus was largely on the medication with little discussion about the provision of psychological support and psychosocial activities. Over time, the discourse surrounding Buvidal has shifted. Stakeholders and patients are now adopting a more balanced view, increasingly recognising that Buvidal is not a panacea or silver bullet, but a tool that must be part of a broader treatment approach.

4.3. Availability and acceptability

Buvidal was first introduced in Wales in 2019 as part of several pilot projects in different parts of Wales. This early work produced positive results, which played a key role in securing national funding for a wider roll out at the start of the pandemic in the spring of 2020. At that time, services were limiting attendance at clinics (to help prevent the spread of the virus) by prescribing large quantities of take-home OST (to provide continuity of care to patients). A monthly injection of Buvidal was an attractive alternative in offering a far safer way of providing continuity of care while minimising attendance at clinics. The importance of stopping the spread of the virus was acknowledged, but there was some concern that the pandemic was driving the treatment offer with little recognition of individual needs.

The urgency of the pandemic enabled the rapid implementation of Buvidal that many believed would not have been possible in normal circumstances. Stakeholders suggested that outside of the pandemic, introducing a new form of treatment would have taken far longer and been much more structured. Some had concerns about how rapidly and widely Buvidal had been rolled out without the traditional checks and balances that would have taken place. Nevertheless, it was widely recognised that the pandemic created an enabling environment where funding requests for Buvidal were perceived as relatively minor amid broader and greater pandemic spending.

The speed of developing Buvidal services varied across Wales with third sector services getting up and running more quickly than NHS services due to their nimbleness and freedom from statutory processes and procedures. However, Buvidal is now available in all seven health boards in Wales, primarily delivered through NHS services either independently or alongside third-sector organisations, with the exception of one area where Buvidal is delivered solely by the third sector. General practitioners are also involved in certain areas, through shared care or primary care models. However, disparities in provision remain.

Some areas offer widespread access, while availability in other areas is more limited. This ‘postcode lottery’ extends to the prison estate, where access varies across institutions, with some providing limited or no access at all to Buvidal. The reasons for this are unclear but availability within the community post-release appears to be a key factor in driving access to Buvidal while in prison. The use of methadone as a tool for encouraging compliance with prison regimes is another possible contributory factor. Despite some logistical challenges,

prison-based Buvidal prescribing offers several benefits, including time savings for patients, reduced risks of diversion, and reducing disorder in methadone queues.

While Buvidal is available in all health board areas, access to the treatment is not always as quick as it might be (and often it is well beyond the Welsh Government's KPI of starting treatment within 20 working days of referral – Digital Health and Care Wales). Waiting lists are common in some areas and these appear to be driven by increased demand for Buvidal via word-of-mouth through peer networks, as well as by improved treatment retention, which has slowed the progression of patients through services. The positivity surrounding Buvidal has led to some clinicians feeling under pressure to prescribe it to patients who might not be eligible.

Rapid access to Buvidal treatment is possible for certain populations and some individuals have reportedly engaged in criminal activity to speed up access to Buvidal through the criminal justice system. A broader issue is the inequity between England and Wales. For example, women who are returning to Wales upon release from English prisons are more likely to be prescribed Buvidal than those remaining in England. Similarly, men returning to England on release from Welsh prisons are less likely to be prescribed Buvidal than those remaining in Wales. The availability of Buvidal in the community plays a key role in the decision to prescribe it in the prison setting.

4.4. Funding and commissioning

Ring-fenced funding (£3m) for Buvidal is issued annually by the Welsh Government to APBs for Buvidal on top of their Substance Misuse Action Fund (SMAF) allocations. As Buvidal is more expensive than other OST, a straightforward reallocation of existing funds was not viable. The funding from the Welsh Government for Buvidal pays only for the medication, which means that all other costs (e.g., administration, psychological support, psychosocial activities, Home Office licences, storage, transportation) must be decided and paid for locally out of other budgets.

The amount of funding allocated to each APB is based on estimates of potential demand, made by providers early in the pandemic when there was little understanding among most (but not all) providers as to how Buvidal might work as a form of OST. These early allocations have not changed over time, despite huge changes in awareness, understanding, and demand.

To meet the increasing demand for Buvidal, with support and encouragement from the Welsh Government, APB commissioners have used slippage from their SMAF budgets at the end of the financial year, to top up their Buvidal funding. Some areas have used the slippage to pre-purchase Buvidal, which involves lodging money with the manufacturer that can be drawn upon as necessary. This process has been useful in enabling APBs to spend money in the appropriate financial year and avert the need to stock large supplies of Buvidal in compliance with strict Home Office regulations. In some areas, the pre-purchasing process has been done by the local authority and in others it has been facilitated by third sector services. This is because pre-purchasing is not permitted under health board rules. There are also benefits in VAT terms as local authorities and charities can claim back the VAT, unlike health boards.

In addition to the annual £3m of ring-fenced funding for Buvidal, the Welsh Government uses underspend from other budgets to fund Buvidal in prisons. Initially, this funding was channelled through the APBs, but it is now allocated centrally. Recent figures show that the Welsh

Government has been funding Buvidal for men in three of the five Welsh male prisons and for women in one English prison. Funding was also allocated by the Welsh Government to a second women's prison in England for 2023/24, but this was discontinued when no further requests for funding were received from the prison.

The two male prisons in Wales where Buvidal is not funded by Welsh Government include one where a small number of prisoners are prescribed Buvidal that is funded by the health board and another where no form of OST is prescribed to any prisoners.

4.5. Administering Buvidal

As a Schedule 3 controlled drug, Buvidal requires administration by two registered nurses: one to administer and another to verify. This requirement presents logistical challenges, particularly for services operating in rural areas and/or with smaller teams. In some areas this has been mitigated, with health board approval, by training support workers to fulfil the role of a registered nurse. However, this practice is costly and not well publicised, meaning that many services continue to face this problem. Improved communication (e.g., through a community of professional practice) could ensure better information sharing, although some recommended a broader relaxation of the rules to remove the requirement altogether.

Only suitably trained professionals are authorised to administer the injection to patients. During the early phase of the pandemic, this requirement created problems due to a lack of experienced injectors within services. Over time, this problem has resolved, and it is now primarily nurses who are responsible for administering the injections. Most, but not all, patients reported having some choice in the injection site (e.g., arm or leg). There was broad agreement among patients that some staff were more competent at administering the injection than others in terms of the amount of pain they experienced. Some patients believed the injection technique influenced the duration of the dose's effect, perhaps because of liquid escape when not injected properly.

4.6. Initiation and maintenance

Thorough medical and psychiatric assessments are considered important before initiating Buvidal due to patients' reports of increased mental clarity and resurfacing trauma. However, concerns were raised that these assessments are sometimes insufficient or omitted altogether.

Initiation practices vary across services with some utilising the Bernese method of microdosing buprenorphine alongside methadone to enable faster and less disruptive transitions, especially for those struggling with dose reductions. However, the more common approach involves tapering methadone to 30ml, followed by a challenge dose of Espranor and a weekly dose of Buvidal.

Dosages depend on a patient's heroin use history, with heavy users often starting on 24mg weekly, later transitioning to 96mg monthly. While some services shift patients to monthly doses rapidly, others maintain weekly doses longer to ensure that patients are fully stabilised before moving to monthly administration. In some services, patients are stabilised on oral buprenorphine before transitioning to weekly and monthly Buvidal injections.

In prison settings, weekly dosing is more common and preferred among prisoners. Within community settings, weekly doses of Buvidal tend to be short-term unless patients are involved with the criminal justice system, when weekly injections are a useful way of maintaining contact.

4.7. Additional support

The frequency of contact with patients varies across services, ranging from weekly to six-monthly, although one patient described a planned move to annual check-ins. There were mixed views on whether the amount of contact with patients was sufficient, with some describing how the shift to monthly rather than daily (or near daily) contact led some patients to become isolated and bored.

While some services offered more support than others, there was broad agreement that a one-size-fits-all approach was not appropriate. Indeed, weekly check-ins were understood to be important for some patients but not necessary for others. The consensus was that a tailored approach, agreed between patient and staff, was appropriate.

The way in which services have responded to the mental clarity and emotional effects of Buvidal varies across areas. Some have invested in psychological support and intervention services, while others have adapted their services by employing trauma specialists. Others have drawn on resources delivered as part of existing contracts.

There is broad consensus on the need for skilled staff to deliver appropriate psychological interventions and for the provision of activities that support meaningful engagement, particularly for those with long histories of illicit opioid use spanning decades whose daily routines previously revolved around substance use. However, some patients declined the opportunity of receiving additional support, citing satisfaction with the medication and a desire to avoid former drug-using networks within service settings.

4.8. Eligibility

At the start of the pandemic, Buvidal was rolled out rapidly across Wales to help prevent the spread of the virus and ensure continuity of care among OST patients. Initially, there were mixed views on what populations would benefit most from Buvidal treatment. Some thought it was most suitable for clinically stable patients and those able and motivated to engage. Others believed it was most suitable for less stable patients who were not doing well on existing treatments.

Early guidance from the Welsh Government recommended prioritising certain populations, including those for whom it was clinically safer than other forms of OST, people who were homeless, and people with complex needs. Initially, the primary aim was to help keep people safe from both the virus and drug-related harm. The idea of using Buvidal to help move patients on in their recovery came later, once evidence of its effectiveness across a range of health and social outcomes had emerged.

As restrictions eased, local services established their own eligibility criteria. Some services now prioritise certain populations, notably vulnerable groups such as victims of domestic violence, individuals with overdose histories, and those with mental health challenges. Patients

who are parents are another priority group, given that a monthly injection removes the need to store opioids in the home (putting children at potential risk) and increases flexibility for childcare, employment and family holidays. Some services prioritise patients based on their proximity to services, as monthly injections reduce the need to travel long distances to services, saving patients both time and money.

There is broad consensus among stakeholders and patients that both stable and non-stable individuals can benefit from Buvidal. However, concerns persist over prison-based inequities, with eligibility driven largely by the availability of Buvidal in the area where patients will be living post release. Concerns have also been raised in community settings due to some services prioritising service-level needs by using Buvidal as a tool to minimise the attendance of disruptive patients. Overall, most stakeholders and patients agreed eligibility for Buvidal should be guided by clinical need, patient choice, and motivation to engage.

4.9. Guidance and training

The early roll out of Buvidal was described as somewhat frantic, with little formal guidance and a largely reactive approach to the onset of the COVID-19 pandemic. Those involved in pilot projects prior to the pandemic reported receiving training on Buvidal from the manufacturer. Others, however, had little information to guide them. Guidance that was given included messages to disregard licencing guidelines and shift patients straight to monthly injections, rather than stabilising them for longer periods on weekly doses. Stakeholders described being left largely to fend for themselves at that time, a situation with which some were uncomfortable.

Over time, confidence has grown through practice and peer support, with many services developing their own internal guidance for staff and patients. However, silo working within services and health board areas is evident across Wales, meaning that opportunities to share best practice and optimise service delivery have been missed (e.g., use of the Bernese method of microdosing for induction, and training healthcare workers to perform the role of a second registered nurse).

Stakeholders were keen for more guidance, especially around pain relief, engagement strategies, and side effects, identifying a need for training in key areas, including: the pharmacological and psychological effects of Buvidal; supporting patients in avoiding other substances; managing treatment duration and detoxification; and responding to reports of lack of effect.

A standardised training module, potentially through the Royal College of General Practitioners (RCGP), was recommended as a possibility. Patients also expressed a desire for better information on what to expect, and for staff to be trained in minimising the pain of the injection and injection-site reactions.

4.10. Licence requirements

As a Schedule 3 drug under the Misuse of Drugs Regulations 2001, Buvidal presents several administrative and financial challenges to services. Licencing was particularly burdensome during the early stages of roll out, causing delays in getting some services up and running.

Licencing rules remain a challenge, with some services relying on community and hospital pharmacies to store Buvidal on their behalf, creating logistical complications and increased work for pharmacy staff. Furthermore, individualised labelling of Buvidal doses means missed appointments require doses to be returned (which wastes time) and destroyed (which wastes money). In prisons, individualised labelling and dispensing requirements make Buvidal more labour-intensive than methadone.

Licencing requirements are not only logistically challenging, they are also financially challenging. This is because licences must be acquired for each service location, incurring costs that must be met within existing budgets. Additional expenses include the costs of conducting Disclosure and Barring Service (DBS) checks, installing alarms, and complying with safe storage requirements.

Views on the necessity of stringent licencing requirements were mixed. While misuse and diversion potential was widely recognised as very low for Buvidal, the unanticipated diversion of other medications (e.g., blood thinners) was highlighted as an issue to be mindful of.

4.11. Exiting treatment

There was a consensus among participants that patients were not under any pressure to exit treatment within any specified timeframe, and agreement that this would not be in their best interests. Premature exit was considered potentially harmful and could result in relapse and a return to treatment.

The number of planned exits from Buvidal treatment varied across services, with some noting very few and others many more, including up to 30% of patients in some primary care settings. The higher rate of successful exits among patients in such settings is likely to be because they tend to be further along in their treatment journeys than those in specialist services. Accessing Buvidal through GPs was viewed positively, with benefits including reduced stigma and freeing up capacity in specialist services.

5. Impact evaluation

- An impact evaluation was conducted to assess the effectiveness of Buvidal drawing on the perspectives and experiences of stakeholders and patients.
- Buvidal is widely perceived as an effective form of OST, praised for its ability to reduce cravings and withdrawal symptoms, block opioid effects, and improve quality of life. It was often described as a game changer and life changing.
- Patients valued the sustained release, mental clarity, and freedom from daily clinic visits, reporting improvements in relationships, employment, education, and psychological wellbeing.
- While some experienced emotional challenges, mild withdrawal, isolation and boredom, Buvidal was largely seen as more effective than other OST options, with minimal side effects and high retention rates.
- Other benefits included reduced (but not eliminated) overdose risk and easier tapering compared to other OSTs, though stakeholders cautioned against imposing time limits on treatment.
- When delivered as part of a broader package of care including access to professional psychological support and psychosocial activities, Buvidal presents an effective treatment option that supports both long-term maintenance and gradual, supported detoxification when patients are ready.

5.1. Introduction

A key aim of the evaluation was to provide the Welsh Government with an indication of Buvidal's overall effectiveness, including any differences between outcomes for those on Buvidal and other forms of opioid substitution treatment (OST). To achieve this aim, we conducted an impact evaluation drawing on data collected from professional stakeholders (through semi-structured interviews and an online survey) and from patients (through focus groups).

The findings from the impact evaluation comprise a separate output. Here, we provide a summary of the report focusing on a range of health and social outcomes experienced by patients on Buvidal (see Annex Figure 5.1 for an overview). The themes covered in this chapter include: perceptions of effectiveness and cost-effectiveness; abstinence from opioids and other substances; withdrawal and cravings; overdose and death; psychological, physical and social outcomes; retention in treatment; side effects; experiences of stigma; and the process of 'coming off' Buvidal.

5.2. Perceptions of effectiveness

The discourse surrounding Buvidal was overwhelmingly positive with most stakeholders and patients perceiving it to be an effective form of treatment. There was broad agreement among them that Buvidal is more effective than other forms of OST. A key benefit of Buvidal is that it restricts on-top use of opioids, due to it being a partial agonist and opioid blocker. Methadone as a full agonist, however, more easily permits on-top use and is used by some patients either as a back-up if heroin cannot be bought or as currency with which to purchase street drugs.

While people on daily (or near daily) OST are often taking it to prevent withdrawal, there was a sense that many people on Buvidal were trying to achieve opioid abstinence and move on in their lives. The broad consensus among stakeholders and patients was that while not suitable for everyone, for many, Buvidal is a 'game changer' that can have life-changing effects.

5.3. Abstinence

5.3.1. Abstinence from opioids

A key goal of any form of OST is to substitute the use of illicit opioids with use of a prescribed pharmaceutical alternative of known purity and strength (Public Health England, 2021). The use of opioids on top of Buvidal was rarely reported, largely because patients know that it is a 'blocker', and do not want to waste their money on something that will have no effect. Nevertheless, some patients were curious and tested the theory by using opioids on-top of Buvidal. Others did this at the start of treatment in fear of the emergence of painful withdrawal symptoms. When no opioid effects were felt, patients stopped using on-top.

Patients described the benefits of knowing about the blocker action of Buvidal, which they saw as a safety net protecting them against relapse. Some staff promoted the idea to patients that using on-top was pointless. Others, however, warned patients that overdose was still possible with strong opioids and/or large quantities of heroin. This was confirmed by patients who reported that they had 'broken the blocker' with fentanyl and 'copious' quantities of heroin.

That opioid overdose is still possible on Buvidal creates a dilemma for services. Is it appropriate that staff discourage on-top opioid use by advising patients that it is a waste of money? Or should they warn patients that opioid overdose is possible and issue naloxone kits as a precaution? The latter would appear to be more in line with a harm reduction approach, which is important at a time when nitazenes are becoming increasingly prevalent in the UK (Holland et al. 2024).

Most stakeholders believed on-top opioid use had decreased or stopped among most Buvidal patients, including those described as 'chaotic'. However, use of opioids was noted among some, which was attributed to the ritual of drug use and being stuck in a habit of needing something every day. The social context of daily drug use was also identified as a driver of on-top opioid use.

5.3.2. Abstinence from other substances

Discussions around abstinence from other substances tended to centre around the use of crack cocaine, though references to alcohol, cannabis and benzodiazepines were also mentioned. There was no clear pattern in relation to the on-top use of other substances, with some patients reporting that their use had slowed down or ceased and others reporting increases. Increases were linked to having more time and money available to spend on other substances, as well as to the resurfacing of emotions and the need to dampen those feelings. Some patients also reported the need to fill the void left now they had stopped using heroin. The positive impact of psychological support was noted in helping Buvidal patients to stop relying on substances to cope with historic traumatic experiences.

While the use of crack on top of Buvidal was reported by many participants, the practice was not thought to be widespread among all patients and when it did occur it was typically among

those with histories of using crack. There was some suggestion that the discourse surrounding the increase in crack use had become scripted, as in hearsay, rather than grounded in evidence or personal experience, and that perhaps the change was no different to that seen with other forms of OST. There was also the possibility the increase was not due to Buvidal, but the result of a general increase in the availability of cocaine across the UK.

5.4. Withdrawal and cravings

Avoiding the pain of withdrawal is a key motivator for the continued use of illicit opioids. By providing a safer prescribed pharmaceutical substitute, OST helps to keep withdrawal symptoms at bay and thereby prevent the continued use of illicit opioids (Public Health England, 2021). Patients reported a notable lack of withdrawal symptoms while on Buvidal, which came as a surprise to some and resulted in some forgetting to return for their next dose. Nevertheless, the fear of withdrawal was significant among some patients who reported they could feel withdrawal coming on towards the end of their dosing window. This fear led to some reluctance to move from weekly to monthly doses.

The extent to which feelings of withdrawal were real or anticipated was debated among stakeholders and patients. Some speculated it might be psychological and the result of ingrained habits of using drugs daily. Others attributed the feelings of withdrawal to a stress response, which was confirmed when patients started to feel better minutes after being given an 8mg booster dose, which would have taken hours to peak rather than minutes. However, not being believed was an issue for some patients who commented on how the positive discourse surrounding Buvidal led some staff to disregard their reports of withdrawal.

The possibility that some patients might not do well on Buvidal was raised given the experiences of a small sub-group of patients who reportedly felt an increase in withdrawal symptoms at higher doses of Buvidal.

In much the same way that it helps prevent withdrawal, OST also helps to stop cravings (i.e., the overwhelmingly strong desire or need to use opioids). As noted in relation to withdrawal, many patients reported that Buvidal had also stopped or reduced their drug cravings. This included patients who had not experienced cravings from the moment they started Buvidal and patients who had not been triggered when in the presence of other people using drugs. Stakeholders also reported witnessing a lack of craving among patients and attributed this to two key factors, namely: a sustained high plasma level of buprenorphine, rather than the up and down of short-acting opioids such as heroin, methadone and oral buprenorphine; and a change in their social context.

5.5. Opioid overdose and death

An important feature of OST is that it involves the substitution of an illicit opioid of unknown strength and purity with a prescribed alternative where the dose is known, and the risk of overdose and death is reduced. That Buvidal offered protection from overdose was a widely held belief among stakeholders and patients and there was a belief that the number of overdoses had reduced since the implementation of Buvidal. Most participants reported they did not know of anyone who had overdosed while on Buvidal. It was on only a small number of occasions that opioid overdoses were experienced by patients on Buvidal, including one patient who had overdosed on fentanyl. The main conclusion to be drawn is that while Buvidal

appears to offer some protection from overdose, the risk is not eliminated, particularly if patients are using strong opioids or opioids in large quantities.

There was a broad consensus among patients and stakeholders that Buvidal was contributing to fewer deaths among people who use opioids. Aside from its blocker activity, Buvidal was also understood to have contributed to a decrease in drug-related deaths through reducing the amount of illicit methadone and oral buprenorphine on the street. Some stakeholders reported that when deaths did occur, they were often the result of an illness and other comorbidities. There was also a suggestion that deaths were less likely to occur among patients on Buvidal than on methadone because of the risk of overdose on methadone.

5.6. Psychological outcomes

A recurring theme raised by many participants, was the clarity of mind that patients experienced when on Buvidal. Descriptions of this were vivid and included a wide range of experiences. For some patients, the impact of this clarity was positive as it enabled them to focus on their treatment, live a daily life and step away from addiction. For others the experience was not wholly positive, and in some cases, it was acutely problematic. The main drawback for some was unmasking trauma that had been hidden deeply behind years of opioid use. However, being clear-headed also meant some patients were confronted with the reality of their poor living conditions. Stakeholders were in broad agreement that many patients could not deal with and/or were not ready for this clarity of mind. For patients struggling to cope, there was a risk they would turn to other substances (e.g., crack, benzodiazepines or alcohol) to cope with their emotions.

The numbing effect of methadone was described as very different to the clear-headedness of Buvidal. Patients also described differences between Buvidal and oral buprenorphine, which is interesting given both are forms of buprenorphine. One explanation for this could be that some patients on oral buprenorphine use substances on-top, preventing clarity of mind from developing. Another explanation is linked to the routine of daily pick-up from services, filling patients' time, and stopping them thinking about their past traumas. There was agreement among stakeholders that with the right service structure and appropriate psychological support, clarity of mind can be managed, and patients can be supported to achieve positive outcomes.

Buvidal was also linked with several other psychological outcomes, including the development of a new positive 'non-addict' identity. This change in identity was linked to being free from the routine of daily pick-ups, to the safety net that Buvidal provides as an opioid blocker, and to a life free of worry about sourcing illicit drugs. Changes in anxiety and depression were also mentioned, albeit rarely with participants describing mixed experiences including increases and decreases.

Importantly, a small number of patients mentioned Buvidal had negatively affected their mood and led to suicidal ideation during the early stages of treatment. It is conceivable that such mood fluctuations are linked to clarity of mind and the resurfacing of emotions. However, an alternative explanation was offered by one stakeholder who reported that a small group of patients with pre-existing mental health conditions felt ill on Buvidal.

5.7. Physical health outcomes

Buvidal was linked by participants to a range of physical health outcomes, the majority of which were positive. One commonly reported outcome was a change in physical appearance with stakeholders describing ‘profoundly changed’ patients who they barely recognised in the waiting room. Changes in weight were often mentioned, including both increases and decreases. Weight gain was linked to an increase in appetite, which was explained in several ways including, an increase in the use of cannabis and a decrease in the sniffing of oral buprenorphine. Weight loss was linked to having more time to engage in healthy activities.

Buvidal also gave patients the time and space to deal with ongoing health problems. Being on Buvidal resulted in patients prioritising health concerns that had previously been at the bottom of their list. For some, this meant they received diagnoses of serious health problems, the pain of which had been suppressed by the continued use of opioid agonists such as heroin. For some patients, being on Buvidal rather than heroin meant they became aware of normal bodily functions, such as menstruation, which they did not always like.

5.8. Social outcomes

A range of important social outcomes were observed among Buvidal patients. Chief among these was the opportunity to break free from a drug-using lifestyle, which many patients had been living for years if not decades. One of the main ways in which Buvidal facilitated this freedom was by breaking the cycle of attending pharmacies and clinics, which reduced opportunities to bump into members of their former drug-using networks, and of being triggered by memories of their previous lives. In practice, the monthly schedule of attendance was more forgiving, enabling patients who missed appointments due to unforeseen events to remain in treatment rather than be exited for non-compliance.

While a break from daily attendance was positive for most patients in giving them their freedom back, it was recognised that some patients struggle with the change in daily routine. For some, more frequent appointments are useful in providing routine and structure to otherwise hectic lives.

Buvidal was described as enabling patients to live ‘normal’ lives, whereas the use of daily OST was likened by some to an addiction that made patients feel like they were still using. However, some patients found comfort in knowing that they were taking medication on a daily basis.

The words ‘life changing’ were often mentioned by participants in relation to Buvidal. For many, removing the need to attend clinics every day, helped improve the quality of their lives. It gave them more control over their lives and led to improvements in their social lives, including the ability to travel and go on holiday more easily. With more time on their hands now that they were not having to travel to clinics every day, patients also began to take up new hobbies and rediscover old ones.

While an improved quality of life came easily to some patients, for others it was possible only with professional psychological support and psychosocial activities. This was because the amount of free time on their hands meant that they became bored, isolated, and needed help in finding meaningful occupation to prevent relapse.

Many participants commented on the positive impact of Buvidal on helping patients enter employment, training and education (ETE). The ability to engage in ETE was often linked to the reduction in daily clinic visits, although clarity of mind also played a role. Even patients with no history of prior employment reported positive ETE outcomes as a result of Buvidal treatment.

Improved relationships with family members were also evident among Buvidal patients. This included those able to rebuild bridges with estranged family members and patients who regained custody of their children. There was a sense that Buvidal was far more effective than other forms of OST in facilitating relationships and helping patients reconnect. A key facilitator in this regard was the time and space patients now had to be more present with their children rather than attending clinics so frequently. There was also a suggestion patients were more alert and better able to look after their children. Being on Buvidal also meant there was no methadone or buprenorphine in the house presenting a danger for children and animals.

Importantly, having Buvidal in their system was also useful in enabling victims of domestic violence to move out of an area quickly without needing to worry about going into withdrawal while trying to sort out where to get their script. Having Buvidal in their bodies also meant that abusive partners were not able to control their daily doses of OST (e.g. by coercing them into sharing or diverting their medication). A key drawback of this, however, was that some patients were at risk of violence from frustrated partners who did not want them to be on Buvidal.

While Buvidal clearly helped many patients experience improvements in their relationships, there was also evidence that some became isolated and lonely given their reduced contact with society. For some, this change in routine was understood to be destabilising, with stakeholders suggesting that the varied responses to Buvidal need to be acknowledged more widely.

The impact of Buvidal on people's accommodation status was not commonly discussed among patients or stakeholders. When it was mentioned, however, the comments were positive and referred to improvements in housing status, some noting patients maintaining tenancies for the first time in their lives. Stakeholders attributed improvements in housing to the clarity of mind that Buvidal brought to patients, providing stability and enabling them to think about their housing situation. As with other outcomes, Buvidal appeared to outperform other forms of OST.

5.9. Treatment retention

Research shows that longer treatment times are associated with better health outcomes (Villamil et al. 2024). Buvidal patients experienced better rates of retention in treatment than patients in other forms of OST. This superior retention rate was attributed to the flexibility and autonomy that Buvidal affords to patients. However, this flexibility was recognised to be a double-edged sword as for some patients it resulted in reduced contact with services.

Most patients were happy to remain on Buvidal, and it was reportedly rare for patients to request a return to other forms of OST (a finding also reported in our analysis of the SAIL data). When a switch was requested, this was typically due to being unable to cope with the clarity of mind, a change in emotional state and the need to take a drug every day. Daily use helped patients deal with the fear of withdrawal, providing them with a daily routine and contact

with the outside world. There was a suggestion that sometimes healthcare providers were reluctant for patients to make the switch back and it was recommended that a return to other forms of OST should be an option for those ‘slipping back into the mindset’ of needing take something every day

5.10. Side effects

Buvidal was reported to have several unintended side effects, most of which were low level, notably those linked to the physical administration of Buvidal, including the pain and sting of the injection. The amount of pain experienced was linked to the injection technique used, with some administrators believed to be more effective than others. The degree of pain felt was also reported to be linked to colder temperature and to whether the dose was weekly or monthly.

Lumps at the injection site were commonly reported, although these were largely unproblematic, rarely painful, and did not require further medical treatment. The main drawbacks of the lumps were that they were sometimes noticeable and some reported being concerned that their partners might notice them and realise they were on Buvidal. However, the sting and lumps were not always unwelcome as they provided reassurance to some patients that the medication was in their bodies.

Other side effects included infrequent reports of bruises, rashes, and reactions at the injection site. On very rare occasions these required treatment with antihistamines. Other infrequent side effects included some patients getting a ‘high’ shortly after being injected. There were also occasional reports of headaches that were not relieved by standard pain medications, issues with temperature regulation, with some feeling too hot and others very cold, and changes in sleeping patterns, with some experiencing problems and others sleeping more soundly. In addition, there were reports of increased anxiety in the form of panic attacks, which were linked to the resurfacing of emotions and the clarity of mind described above.

5.11. A solution, but not a silver bullet

There was broad agreement that while Buvidal was ‘life changing’ for many patients, it was not a cure-all, and hence not a silver bullet that would solve opioid dependence completely. This was because there were some groups on Buvidal for whom it was not suited, who did not like it, and who did not do well. Perhaps due to trauma or other reasons, it was recognised that some patients wanted to continue using heroin, making Buvidal (as a partial agonist and blocker) an unsuitable choice. For this group it was recognised that other forms of OST were important and helped minimise the harm associated with illicit drug use.

While mindset was widely acknowledged to be an important ingredient for success, there was a counter view that Buvidal was effective even among those who were less stable and not engaging well in treatment. However, it was suggested that Buvidal might not be suitable for patients with certain illnesses, such as major mental health conditions like schizophrenia, who might be better treated with methadone given its sedative properties.

5.12. Stigma

People with opioid problems are one of the most vulnerable, marginalised and stigmatised groups in society (Cheetham et al., 2022). Importantly, Buvidal has helped to address this stigma in several ways including: reducing opportunities for stigmatisation by reducing the need to visit pharmacies and clinics from daily to monthly; reducing self-stigma through a change in identity with patients no longer labelling themselves as 'addicts' or 'drug users'; and by helping to demonstrate to healthcare professionals that this population of patients are no different to any other and not difficult to treat. While a reduction in stigmatising experiences was reported, stigma was not eliminated. Indeed, as OST patients, some of those on Buvidal reported being treated poorly in certain healthcare settings.

5.13. Prison outcomes

Buvidal was reported to offer several benefits to prisons. Chief among these was that unlike methadone and oral buprenorphine, it was not possible to misuse or effectively divert Buvidal. That said, attempts to divert were reported in a small number of cases. There were also reports of patients trying to capture liquid that sometimes get excreted when Buvidal is injected.

Another key benefit of Buvidal in prisons is the logistical benefits it provides. Methadone can be challenging to distribute if it requires the mass movement of people around a prison. Furthermore, the process of administering methadone is time consuming and labour intensive, whereas Buvidal can be administered more efficiently. In prisons, most patients receive their methadone by queueing at a medicine hatch. These queues are often long, leading to frustration and potentially the onset of withdrawal symptoms. As such, methadone queues can be breeding grounds for violence and bullying.

The logistical benefits offered to prisons by Buvidal were not universally recognised, with some reporting their workload had increased with more patients in total accessing OST. Furthermore, while administering Buvidal was simpler in some respects, it was more complicated in that each dose needs to be labelled for a specific patient, which is more time-consuming than sending methadone in bulk to the wings.

Putting patients on Buvidal in prison was seen as advantageous in that continuity of care was easier to organise and patients no longer needed to worry about sourcing OST upon release. In addition to reducing the risk of relapse, this also helps prevent an opioid overdose, given the period immediately following release from prison is a period of increased risk of drug-related death (Borschmann and Kinner, 2021). However, as community services need to accommodate prison leavers, this can limit access to non-criminal justice patients.

5.14. Cost effectiveness

Many commented on the lower cost of methadone relative to Buvidal, although some challenged whether methadone really was cheaper once the accumulative costs of dispensing and supervision are considered. Others highlighted the hidden costs of delivering Buvidal, including the costs associated with the strict controls governing the storage, transport and administration of a controlled Schedule 3 substance.

A small number of stakeholders were dubious about whether Buvidal offered good value for money. However, most participants suggested the life-changing outcomes experienced by most Buvidal patients were worth the investment. It was widely believed these positive outcomes had led to huge cost savings across a range of domains (e.g. physical health, mental health, crime, employment, relationships, finances) and in some cases to income generation through paying taxes as a result of employment or car ownership.

While it was widely believed that Buvidal was 'worth it', there was also recognition that to maximise its effectiveness and achieve its full potential, more than the injection is required. There was broad agreement that psychological support (delivered by qualified staff members) and psychosocial interventions should be available for those in need, as they should also be for patients on other forms of OST.

While the costs may on the face of it seem high, some stakeholders challenged this conclusion, highlighting the role of stigma in decisions surrounding the funding of Buvidal. Stakeholders were concerned that patients with drug problems were not thought worth spending money on and frustrated that they were treated less favourably than other patients (e.g. oncology patients).

5.15. 'Coming off' Buvidal

An important measure of a treatment's effectiveness is the extent to which patients complete and exit that treatment successfully. When asked if Buvidal was time limited in any way, there was a broad consensus that patients were not under any pressure to 'come off' Buvidal within any specific timeframe, suggesting it is being used largely as a form of maintenance treatment. However, there were concerns that if funding for Buvidal was reduced then time limits might need to be introduced to make space for new entrants.

In practice, there were many reports of patients who had chosen to come off in a planned fashion, as well as those who had done so unintentionally. There were also reports of patients specifically wanting to use Buvidal to come off opioids. In such cases, Buvidal was used as tool to assist detoxification. There was a clear sense that coming off Buvidal was smoother and far easier than coming off methadone or oral buprenorphine.

Importantly, seeing other patients come off Buvidal encouraged other patients to follow suit. Nevertheless, the fear of withdrawal is powerful and some patients, even those motivated to come off Buvidal, were nervous about stopping their treatment. To help alleviate this anxiety, there was the option of tapering down the dose before coming off it completely.

The fear of losing their treatment space was a concern for some patients, preventing some from starting the process. The practice of accepting patients back into treatment (bypassing any waiting list) was a solution to this fear, but the extent to which this was an option available indefinitely, or in all areas, was not clear.

6. Analysis of healthcare activities and costs

- Data from the Secure Anonymised Information Linkage databank were used to compare the health outcomes of patients on Buvidal with the outcomes of patients on other forms of Opioid Substitution Treatment.
- Over the study period (April 2020 to August 2024), 157 all-cause deaths and 80 drug-poisoning deaths were recorded among patients on OST in Wales. More than half of these deaths were among patients on methadone while the remainder were fairly evenly split between patients on Buvidal and patients on oral buprenorphine.
- Buvidal patients were less likely than those on methadone and oral buprenorphine to use the ambulance service and attend emergency departments. They were also less likely to attend GP appointments, to be hospitalised in general (vs methadone) and to have elective hospitalisations (vs oral buprenorphine). These findings may reflect increased stability, improved general health and greater use of outpatient services.
- Buvidal patients were less likely to have received a COVID-19 vaccination but there was no difference in their rate of infection, which may be due to less exposure to the virus at clinics or in street drug markets or due to recording/testing limitations.
- Patients on Buvidal tended to use healthcare services less often than those on methadone and oral buprenorphine, which translates into lower healthcare utilisation costs to the NHS. The difference is most marked in relation to use of the ambulance service where the associated costs were 125% and 100% higher among methadone and oral buprenorphine patients, respectively. These conclusions must be drawn with caution due to inaccurate and missing data. Furthermore, due to the lack of available data and time constraints, the analysis did not account for the reason for the attendance or for the comorbidity of patients, both of which warrant further investigation.

6.1. Introduction

A key aim of the evaluation was to provide the Welsh Government with a summary that would compare outcomes for those on Buvidal with those on other forms of opioid substitution treatment (OST). To achieve this aim, we analysed data contained within the Secure Anonymised Information Linkage (SAIL) Databank.

Detailed findings from our analyses of the SAIL data will be presented in depth in a separate report. Here, we provide a summary of the report highlighting the key findings of the analyses. The analysis focuses on nine health outcomes, namely: mortality; hospitalisation; ambulance service usage; emergency department attendance; outpatient attendance; critical care; GP attendance; COVID-19 vaccination; and SARS-CoV2 infection.

6.2. Methods

The study cohort included all records of treatments of interest (i.e., opioid substitution treatments (OST) - methadone, oral buprenorphine and injectable buprenorphine – Buvidal) referred or started after 1 April 2020. It is important to note that cohort construction was adversely affected by both incomplete and inaccurate records within the substance misuse database. Indeed, we found numerous scenarios which were not plausible (e.g., treatment

journeys where the referral date was after the contact end date and overlapping treatment journeys). To resolve the issues, the data were cleaned by applying a set of assumptions and principles developed with the input of professionals experienced in collecting and submitting data within the substance misuse database. It was not feasible to ask substance misuse services to make amendments given the anonymity of the SAIL data.

6.3. Profile of patients

The final cohort used in our analyses includes 5,030 patients. Focusing on the first treatment journey recorded during the study period, just under three quarters of the patients were male and most of them were between 30 and 59 years old. Patients from all local authority areas of Wales were represented in the sample, although some areas were more heavily represented than others (e.g., Cardiff). The records suggest that 10% of patients were referred into treatment from outside of Wales. However, this is likely to be an overestimate given that, reportedly, this category is sometimes used when the referral location is unknown.

The study cohort includes 9,010 patient journeys and 10,348 treatment records (21% oral buprenorphine, 33% Buvidal and 46% methadone). Many of the patients in the cohort had histories of several different types of OST, including 14% with Buvidal and methadone, 10% with Buvidal and oral buprenorphine, and 5% with all three. Just over one-fifth of patients had a history of Buvidal alone. Within the 9,010 patient journeys, 86% include one treatment episode, while 13% include two. While many patients switched from methadone or oral buprenorphine to Buvidal, there were also journeys showing switches away from Buvidal and back to oral buprenorphine (5%) and methadone (2%). There were also a small number of patients who had more than one Buvidal journey (1%).

Focusing only on those patients who were treated with Buvidal, the group shows a similar demographic profile to the full study cohort, including more men than women, more patients aged 30 to 59 than other age groups, and more patients from Cardiff than any other area.

6.4. Mortality

All deaths during OST and those that happened within three months after the last treatment (i.e., the modality end date) were included in the analysis. The underlying causes of death were extracted from the Annual District Death Extract database. ICD-10 codes used to define deaths related to drug poisoning were taken from ONS (2020). Deaths were grouped by the type of treatment at the time of death or the last treatment before death.

Deaths from all causes were highest among patients on methadone (n=87) and lowest among those on oral buprenorphine (n=33). The number of deaths among patients on Buvidal (n=37) was similar to the number on oral buprenorphine. This pattern was the same for deaths related to ‘drug poisoning’ with mortality highest among patients on methadone (n=47) and lowest on oral buprenorphine (n=14) with a similar, but slightly higher, number of deaths among those on Buvidal (n=19). It was not possible to compare the risk of death between the different types of treatment because there were too many factors that might have influenced the results. These included possible spill-over effects from previous forms of treatment and underlying health conditions that were unknown and hence could not be adjusted for. In addition, switching between treatments is not random, which introduces further confounding and limits our ability to make fair comparisons.

6.5. Hospitalisation

All hospitalisations during treatment were extracted from the Patient Episode Database Wales (PEDW) with the admission date falling between the modality start date and modality end date of a treatment period. Incidence rate ratios (IRR) and corresponding confidence intervals were calculated using negative binomial regression for the indicators included in this report. The results show that those who were treated with methadone were 15% more likely than Buvidal patients to experience hospitalisation during treatment (IRR 1.15, 95% confidence interval [1.01, 1.32]). If a unit cost per hospitalisation is applied, this translates to an estimated 15% higher cost of inpatient care for patients treated with methadone than for those treated with Buvidal. For those treated with oral buprenorphine, the rate of hospitalisation was similar compared with patients treated with Buvidal (1.02, [0.87, 1.21]).

All hospitalisations were further explored by admission method, namely emergency, elective or other[5]. For emergency hospitalisations, those treated with methadone and oral buprenorphine had similar rates of admission as those treated with Buvidal (methadone 0.96 [0.86, 1.08]; oral buprenorphine 0.93 [0.80, 1.08]). For elective hospitalisations, those treated with oral buprenorphine had a higher rate than those treated with Buvidal (oral buprenorphine 1.39 [1.00, 1.94]) while those treated with methadone had a similar rate to those treated with Buvidal (methadone 1.11 [0.86, 1.45]).

6.6. Ambulance service usage

All records of patients attended by Welsh Ambulance Services staff (between April 2020 and November 2022[6]) were extracted from Welsh Ambulance Services NHS Trust (WAST) database. If a patient was seen by WAST staff multiple times on the same day, only one record was kept. The results show that those who were treated with methadone and oral buprenorphine were twice as likely to use WAST as those treated with Buvidal (methadone 2.25 [1.76, 2.88]; oral buprenorphine 2.00 [1.49, 2.70]). These results suggest that the cost of ambulance service use for patients treated with methadone and oral buprenorphine was 125% and 100% higher than for those treated with Buvidal if a unit cost is applied.

6.7. Emergency department attendance

All emergency department attendances during treatment were extracted from the Emergency Department Database Wales. The results show that those who were treated with methadone and oral buprenorphine had a higher rate of emergency department attendance than those treated with Buvidal (methadone 1.25 [1.13, 1.39]; oral buprenorphine 1.16 [1.02, 1.31). If a unit cost per attendance is applied, the results translate into an estimated 25% and 16% higher cost of emergency care for patients treated with methadone and oral buprenorphine respectively, compared with those treated with Buvidal.

Amongst all emergency department attendance, some patients exited with self-discharge. Those treated with methadone and oral buprenorphine had a similar rate of self-discharge to those treated with Buvidal (methadone 1.06 [0.93, 1.22]; oral buprenorphine 1.04 [0.88, 1.24]).

[5] 'Other' includes patients who have been admitted following transfer from another hospital. This may include an elective or emergency transfer from another hospital.
[6] Data beyond this date were not available at the time of writing the report in October 2025.

6.8. Outpatient attendance

All cases of outpatient attendance during treatment were extracted from the Outpatient Database for Wales. The results show that those who were treated with methadone or oral buprenorphine had a lower rate of outpatient attendance than those treated with Buvidal (methadone 0.75 [0.68, 0.82]; oral buprenorphine 0.62 [0.55, 0.69]). The costs of outpatient care for patients treated with methadone and buprenorphine respectively were 25% and 38% lower than those treated with Buvidal if a unit cost per outpatient visit is applied.

6.9. Critical care

All critical care admissions during treatment were extracted from Critical Care Data Set Wales. The results show that those who were treated with methadone and oral buprenorphine had a similar rate of critical care admission to those treated with Buvidal (methadone 1.04 [0.71, 1.51]; oral buprenorphine 0.94 [0.58, 1.50]).

6.10. GP attendance

All GP attendances for all reasons during the treatment episode were extracted from the Welsh Longitudinal General Practice Dataset. Results show that those who were treated with methadone and oral buprenorphine had a higher rate of GP attendance than those treated with Buvidal (methadone 1.15 [1.07, 1.24], oral buprenorphine 1.29 [1.19, 1.40]). These results suggest that the cost of primary care (for consultation only and not including prescriptions) for patients treated with methadone was 15% higher than for those treated with Buvidal if a unit cost per GP consultation is applied. It was 29% higher for those treated with oral buprenorphine.

6.11. COVID-19 vaccination

Information on all vaccinations administered during treatment were extracted from the Welsh Immunisation System when the vaccination date was during a treatment period. The results show that those who were treated with methadone and oral buprenorphine had a higher rate of COVID-19 vaccination than those treated with Buvidal (methadone 1.38 [1.25, 1.53]; oral buprenorphine 1.39 [1.22, 1.58]).

6.12. SARS-CoV-2 infection

All positive tests for SARS-CoV-2 during treatment were extracted from the Laboratory Information Management System Wales. The results show that those who were treated with methadone and oral buprenorphine had a similar rate of infection as those treated with Buvidal (methadone 1.11 [0.81, 1.54]; oral buprenorphine 1.32 [0.90, 1.94]).

6.13. Other outcomes

At the time of writing this report, we are still waiting for access to several datasets - Career Wales dataset, Ministry of Justice datasets and provision of Lifelong Learning data beyond January 2020. Our analyses of these datasets will be presented in a separate report once the data have been provisioned.

7. Theory of change and logic model

- A theory of change (ToC) and logic model for the rapid roll out and implementation of Buvidal in Wales were developed via a staged process, drawing first on team expertise and subsequently on the expertise of stakeholders from across Wales in a series of five workshops.
- The ToC for Buvidal was developed retrospectively given there was no existing theory to draw upon. In practice, two ToCs were developed one reflecting the original aims of the roll out and the second reflecting the aim of reducing drug-related harm.
- Three iterations of the logic model were developed over the course of the evaluation (initial, interim, post-project) mapping out the inputs, outputs and outcomes associated with Buvidal treatment as well as the underpinning assumptions, external influencing factors, and evidence sources.
- Buvidal has emerged as a valuable and welcome addition to the range of opioid substitution treatment options in Wales. In some (but not all) instances, it is seen as a game changer, leading to health and social improvements for many. However, the roll out has also highlighted the importance of properly addressing broader recovery needs alongside the provision of pharmacological treatment.

7.1. Introduction

An important component of the evaluation was to elucidate the theory of change (ToC) for Buvidal and to develop a logic model underpinning the treatment. This process through which we developed a robust, evidence-informed ToC and logic model for Buvidal will be described in full in a separate report. In this chapter we provide a summary of that report, including a brief overview of the methodological approach, an explanation of what a ToC and logic model are, and an overview of the steps taken to develop them. It concludes with visual representation of the final simplified logic model, mapping out the individual elements of the implementation of Buvidal in Wales including the inputs, outputs, and outcomes, as well as the assumptions underpinning its delivery and any external influencing factors.

7.2. Contribution analysis

Contribution Analysis (CA) is one of a group of evaluation methodologies combining practical insights and theory to evaluate complex systems of change (see Livingston et al., 2019 for further details). CA is an approach to evaluation particularly suitable to explore complex, multi-level programmes of work where a direct cause-effect issue (or attribution problem) are rarely possible. In this instance, where long-term changes in drug use behaviour or potential reductions in harm are likely to be the result of a multiplicity of factors. CA researchers explore existing knowledge and gather quantitative and qualitative evaluative evidence from a range of sources to tell the ‘performance story’ about how a particular policy, programme, or service activity is contributing to outcomes in the short, medium, and long term.

7.3. Theory of Change

A ToC provides a comprehensive explanation of how and why a desired change is expected to occur in a given context. It maps the causal pathways from inputs and activities to outcomes, while making explicit the assumptions and contextual factors that underpin the change process.

The roll-out of Buvidal in Wales initially emerged as a public health response to the COVID-19 pandemic, aiming to reduce virus transmission by minimising the need for daily clinic and pharmacy visits. Over time, the focus shifted toward Buvidal's potential to reduce drug-related harms more broadly. This evolution had two key implications for the development of a ToC and logic model:

1. We had to construct an assumed ToC, as no pre-existing or updated ToC was available from the programme's inception.
2. Due to the rapid roll-out of Buvidal in Wales during the COVID-19 pandemic, the delivery programme lacked a clearly defined logic model, requiring us to build one from the ground up.

In following Mayne's (2011) six-step CA model, the starting point was to develop a reasoned theory of change. In essence, this meant taking the given core premise or assumption as the starting point or scaffold for the study. As there was no model prior to the evaluation, the research team had to develop a ToC retrospectively. A further complication was that the current perspective of Buvidal as a treatment contributing to the overall drug treatment provision in Wales did not fully resonate with the primary cause for its initial substantive roll out.

Thus, we established two theories of change, which we have combined within one diagram, with both having the ultimate aim of reductions in harms (see Annex Figure 7.1). The first is what we considered might have been in place for the COVID-19 roll out and the second covers the maintained provision of Buvidal and its contributions to changes in drug-using behaviour and drug-related harm. This is the framework of effectiveness that is the concern of the evaluation as a whole and informs recommendations about the longer-term future of Buvidal treatment in Wales.

7.4. Logic model

Logic models are often used to describe or present theories of change. This is because they provide a clear, structured way to graphically illustrate the detailed programme components as well as the sequence of actions and expected results. Theories of change link outcomes and activities to explain how and why the desired change is expected. A well-constructed logic model is grounded in a solid ToC. In essence, the ToC provides the logic that informs the structure and content of the logic model.

A key aim of the evaluation is to make credible claims about the proposed chain of events in the ToC and to extrapolate these into a logic model. Any claims of credibility for the ToC or the likely contribution of the intervention (availability of Buvidal) to observed outcomes derive from:

1. Evidence that planned activities took place (i.e., funding for, and availability of, Buvidal to prescribers and patients). These are the inputs and outputs of the intervention.

2. Analysis of expected (and unexpected) results using multiple data sources (i.e., has Buvidal delivered the type of results that were expected?). These are the outcomes of the intervention.
3. Consideration of other influencing factors (i.e., what other (external) factors may have affected the availability, uptake, or impact of Buvidal, and alternative explanations for observed changes in drug-using behaviours or associated harms). These are the external factors.
4. Finally, the evidence that supports claims laid out in 1, 2 and 3.

Combined, these considerations become the stages and details of any logic model.

7.5. Methods

The development of the ToC and the associated logic model followed several phases before arriving at the final version. This section provides details of the process followed in each stage. Each iteration of the logic model will be presented in the supplementary ToC report.

7.5.1. Team expertise and knowledge mapping

The process began with a dedicated evaluation team meeting, held prior to any study-related evidence gathering. This session drew on the team's professional and academic expertise to map our initial understanding of why and how Buvidal was implemented in Wales, and what the expected outcomes of this roll out were. We identified and mapped four main strands of theory:

- **External Factors**: Policy, market, and environmental influences
- **Inputs**: Commissioning and prescribing infrastructure
- **Outputs**: Service-level and individual-level experiences of Buvidal
- **Outcomes**: Short, medium, and long-term outcomes

In addition, we also mapped key assumptions and theoretical considerations that would shape Buvidal's implementation and impact.

7.5.2. Initial logic model construction

The next step was to map current and proposed sources of evidence onto the emerging logic model. This helped identify where data already existed, where data were being generated through the evaluation, and where gaps remained.

Three evidence domains were highlighted:

- Existing evidence sources, external to the evaluation: e.g., hospital admission data related to overdose
- Evidence generated through the evaluation: e.g., offending rates from the SAIL database
- Evidence gaps: e.g., perspectives of friends and family members that were not going to be captured in existing databases or our evidence-gathering activities

7.5.3. Interim logic model update

Following the initial mapping, we shared the draft logic model with the Buvidal evaluation project management team within the Welsh Government. We then conducted a series of five stakeholder workshops to test and refine the model. Each workshop followed a consistent format of initial discussion, exploration of Buvidal delivery, and feedback on the logic model.

The workshops were instrumental in improving our understanding of what should be included in the logic model. They also highlighted new areas for further exploration in interviews and focus groups (e.g., the specific needs and experiences of women).

The workshops led to several key updates and additions:

- External factors: Patent duration, competitors and the development of alternative forms of long-acting injectable buprenorphine influencing the manufacturer's ability to supply and dominate the LAIB market.
- Inputs: Regulatory requirements (e.g., Home Office licencing for storage and handling) and the personnel requirements surrounding its sign-out for use were found to be influencing capacity and infrastructure, and uptake of LAIB in Wales.
- Outputs: Patient concerns such as fear of destabilisation when switching from methadone, and stigma associated with injectable substances were found to influence treatment choices.
- Outcomes: Patient reports of improved capacity to manage other physical and mental health conditions while on Buvidal were discussed.

Two new strands were also added:

- Unintended consequences: Individual and service-level consequences of Buvidal implementation were mapped.
- Future directions and challenges: An initial narrative that Buvidal represented an intervention with the potential to change the way opioid dependence management and OST delivery was rolled out in its entirety, with narrative shifts surrounding maintenance and abstinence being possible. However, challenges surrounding the longevity of current innovations were also highlighted (e.g., unknowns surrounding onward funding for Buvidal and equity of support services across patients with opioid problems, not just those receiving Buvidal).

7.5.4. Post-project final logic model and evidence integration

Following the completion of all workshops and the full suite of study-specific work packages, a final update and evidence-mapping exercise was performed. This exercise was based upon stakeholder feedback from all five workshops; evidence from the systematic literature review and from the primary and secondary data strands of the evaluation; and identification of remaining evidence gaps and methodological limitations.

This final iteration of the logic model provides a comprehensive framework for interpreting the evaluation findings and articulating the performance story of Buvidal in Wales. The full evaluation logic model is by necessity a complex diagram. It is designed to capture the phenomena that might be accounting for the observable results. A more simplified version of the final logic model, which excludes the evidence mapping element, can be found in Annex Figure 7.2. It is worth noting the logic model developed for this project was designed for the

purpose of directing and understanding the *evaluation* of Buvidal delivery rather than the actual delivery of Buvidal (i.e., it is an evaluation and not a programme delivery logic model).

An *evaluation* logic model guides and structures an evaluation whereas a *programme delivery* logic model guides and structures programme delivery. It focuses retrospectively on actual implementation and observed outcomes rather than planned future activities and expected outcomes. Furthermore, in addition to inputs, outputs, outcomes, and impacts, an *evaluation* logic model also includes assumptions, indicators, risks and external factors (Perkins et al., 2025).

CA methodologies ultimately require the research team to tell a performance story, and to develop a narrative account of the extent to which what was intended and expected actually happened, and what might account for this. For Buvidal, the performance story might read as follows:

> Buvidal has emerged as a valuable and welcome addition to the range of opioid substitution treatment options in Wales. In some instances, it is seen as a game changer. Its introduction has resulted in health and social improvements for many individuals with opioid problems. However, the roll out has also highlighted a need for greater access to professional psychological support and meaningful psychosocial activities, underscoring the importance of addressing broader recovery needs alongside the provision of pharmacological treatment.

8. The future of Buvidal in Wales

- A model for the future delivery of Buvidal in Wales was developed drawing on the perspectives of patients and professional stakeholders who were (almost) unanimous in their view that Buvidal should continue to be funded.
- Uncertainty around the future funding of Buvidal remains a major concern for services, which risk losing staff, having to cap patient numbers, and reverting to other forms of OST if funding is stopped or reduced.
- The importance of embedding Buvidal into a broader package of care was emphasised, including thorough biopsychosocial assessment, early (and ongoing) access to psychological support and psychosocial activities, and peer support.
- The value of GP shared care services in releasing pressure on specialist services and supporting patient reintegration into the community was widely acknowledged.
- Maintaining high clinical standards was seen as essential, with the need for ongoing service reviews and improvements in data collection practices also emerging as important considerations.

8.1. Introduction

To provide the Welsh Government with guidance on what any future 'new' Buvidal service might look like, we asked stakeholders and patients for their thoughts on the future of Buvidal in Wales. Detailed findings from the discussions will be presented in depth in a separate report. Here, we provide an overview of the main messages under the following broad themes: views on the future of Buvidal in Wales; funding arrangements; GP and community pharmacy involvement; potential locations for delivery; initiation-related issues; peer support; psychological support; provision of psychosocial activities; check-in support; price-related issues; availability of Buvidal; awareness raising, and developing best practice. The chapter ends with a visual representation of a potential future delivery model for Buvidal (see Annex Figure 8.1).

8.2. Views on the future of Buvidal in Wales

Stakeholders and patients were overwhelmingly in support of Buvidal being continued in Wales and were hopeful its funding would continue. The reasons given were based largely on the wide range of positive health and social outcomes experienced by Buvidal patients. These were diverse in nature and included reductions in opioid use, improvements in mental and physical health, relationships, employment, finances and a decrease in offending. Some, patients had started to drive and were now paying car tax. The benefits of Buvidal for particular groups of patients, such as victims of domestic violence, were also recognised and formed part of the rationale for maintaining continued funding for Buvidal. Some participants were keen not only on Buvidal continuing, but on access being broadened, the costs of which would be offset through the positive outcomes noted previously (e.g. improvements in physical health and reductions in healthcare usage).

Stakeholders agreed Buvidal might suit some patients better than others. However, having options was understood to be important and more in tune with treatments for other health

conditions such as high blood pressure, where a range of different medications are available. Some stakeholders couched their support for the continuation of Buvidal behind calls for improvements, particularly in terms of the provision of more robust mental health support.

Participants were in broad agreement that Buvidal should be incorporated into the OST armoury. Stakeholders emphasised the importance of giving patients a choice in their treatment and noted that for a highly stigmatised group such as people with opioid problems, having access to a range of options was essential to support engagement and recovery. There was a consensus that medication alone is not sufficient and that it should be one part of a comprehensive treatment package.

It was also recommended that, notwithstanding resource implications, access to Buvidal should be guided by clinical need rather than by how many spaces are available. Drawing comparisons with treatments for other health conditions, participants stressed the importance of assessing each individual's 'biopsychosocial situation' to determine the most appropriate treatment pathway. To do this effectively, the need for thorough medical assessments before prescribing Buvidal was highlighted. Concerns were raised about disparities across services, with some patients reportedly not having had contact with a doctor for extended periods of time.

8.3. Funding Buvidal treatment

8.3.1. Continuity of funding

Uncertainty over the future of Buvidal was a matter of concern for many stakeholders and patients. At the time of the evaluation (2023-25), it was unclear if funding for Buvidal would be available beyond the 2024-25 financial year. The language used by stakeholders in relation to this was often quite emotive with references to panic, nervousness, anxiety, and fear. Stakeholders were troubled by the negative consequences that losing the funding could have on services and patients. The impact of this was predicted to be massive and damaging due to the need to cut staff, cap treatment spaces, reduce service provision, and switch patients to other forms of OST.

The strength of feeling over the future funding of Buvidal was palpable with stakeholders describing how they would fight tooth and nail to keep patients on Buvidal. Some assessed the idea of stopping the funding as unethical and wrong as well as risky given the positive life changes observed among their patients. One stakeholder went so far as to describe the situation as classic drug-dealing behaviour in that services and patients had now become dependent on Buvidal. Most stakeholders were hopeful that the Welsh Government would continue to fund Buvidal and there were calls for longer-term funding cycles to be implemented. Three-year contracts were viewed far more positively, not only in terms of organisation, but in terms of reducing the frequency of contract reviews and the anxiety associated with recommissioning.

The complexity of the funding of Buvidal and of substance misuse treatment services more broadly, was discussed in the process evaluation. Stakeholders held mixed views in terms of what would work best in the future, although there was some agreement that simplification was necessary. Some thought Buvidal should be funded through the NHS. The possibility of taking funding away from providers and commissioners allocating it on a per patient basis

irrespective of where they are accessing Buvidal was also suggested. Removing specific Buvidal pots was another recommendation.

8.3.2. Price

The higher price of Buvidal in comparison with other forms of OST was of key importance to patients and stakeholders with many looking for ways to ensure its continued availability. One such hope was that the patent on Buvidal would soon expire enabling other manufacturers to compete and drive the price of long-acting injectable buprenorphine down to a more affordable rate. However, it was reported that the multiple patents covering Buvidal are complex and that even when they do all eventually expire (in 2032), replicating the injection delivery system will be no easy task.

Other stakeholders also reflected on the price, including one who reflected back ten years when oral buprenorphine was difficult to access due to its higher cost relative to methadone. This stakeholder predicted that the price will eventually come down as part of the natural cycle of things. While some were optimistic about a price decrease in the long-term, there was concern about the possibility of an increase in the short term. Indeed, one stakeholder was fearful of costs increasing due to the market being 'currently monopolised' by the manufacturer and there being no alternative options available.

8.4. GP involvement

Involving shared and primary care GPs in the delivery of Buvidal more consistently across Wales was supported widely by patients and stakeholders. Patients liked the anonymity that attending a GP afforded, as well as the faster speed of access. Stakeholders were in broad agreement that people can feel stigmatised when attending community drug services and it was recommended that moving patients to GP shared care schemes could help with breaking this stigma. Using GPs for Buvidal treatment was also recognised as useful for addressing the wider healthcare needs of patients, who might otherwise not have seen their GP. As well as benefiting patients, sharing the care of patients with specialist services was described as beneficial to GPs in providing them with reassurance.

While the benefits of involving GPs were widely recognised, several barriers to shared care were identified. One such barrier was that few GPs seemed prepared to get involved. There was speculation this might be due to the costs of setting up a locally enhanced service or due to stigmatised views of people with opioid problems. That one APB area was able to provide shared care very effectively, suggests that with the right infrastructure and leadership, this should be possible elsewhere.

An important benefit of shared care schemes is that it enables patients to move out of specialist services, freeing up capacity to reduce waiting lists and take on new referrals. Without GP involvement, specialist substance misuse services can become blocked up. Indeed, it was noted in both the impact and process evaluation that throughput of Buvidal patients is limited due to high retention rates.

While the main weight of opinion was broadly in support of Buvidal being delivered through shared care arrangements, there were a small number of participants who held reservations.

This included patients who had experienced difficulties accessing GPs in the past and stakeholders who were concerned about the bureaucracy of setting up a shared care scheme.

8.5. Community pharmacy involvement

There were mixed views on the involvement of community pharmacies in the delivery of Buvidal. Those in favour highlighted the benefits in terms of cost savings and the convenience of providing healthcare within local communities and in terms of cost savings to services through averting the need for nurses to transport controlled drugs around and reducing how much is paid to pharmacists for supervised consumption of daily forms of OST.

Those opposed argued it might put patients in the proximity of their former drug-using networks, putting them at risk of relapse. The potential 'triggering' of past pharmacy visits, particularly among those experiencing problems with over-the-counter opioid medications (e.g., codeine), was also highlighted as a drawback to pharmacy involvement. Importantly, while the potential of using community pharmacies was recognised, there were concerns about the lack of support pharmacists would be able to provide, as well as how they would be remunerated for their work. Developing a shared care arrangement with substance misuse services was identified as possible solution to this problem.

8.6. Location of delivery

Several suggestions were made regarding possible delivery options for the future. One idea suggested by a stakeholder was the possibility of self-administration of Buvidal at home in the same way patients self-administer injections as part of their diabetes, IVF, or rheumatoid arthritis treatment. A key benefit of this would be removing the need for staff to administer the injection either in clinics or homes. While potentially beneficial for some patients, the possibility of self-administration was not thought likely, and the stakeholder was concerned about how the media would respond to services issuing syringes containing buprenorphine. The drawback of reducing the amount of contact with services and losing the opportunity to make every contact count was also recognised.

Another suggestion was for Buvidal to be delivered to patients in their own homes, which is already done in some parts of Wales. It was believed that this would remove the need for patients to attend busy services that were struggling to provide minimum standards of accessibility. The benefits of home delivery were noted to be particularly high among those living in rural areas with poor transport links.

Another option was the use of private clinics for the provision of Buvidal. While this was not specifically recommended as a future delivery model, examples of recent use were reported, which highlighted its legitimacy for those with sufficient means who did not want to attend community drug and alcohol services.

Reflecting on Buvidal delivery in the prison context, there was a call for specific Buvidal clinics to operate several times a week. It was suggested this would make it safer for nurses (by limiting their attendance on the wings) and enable wider provision across a larger population of prisoners.

8.7. Initiation

Patients starting on Buvidal are advised that they must be in mild withdrawal prior to their first injection. The reason for this is because buprenorphine is a partial opioid agonist which means that it binds tightly to opioid receptors in the brain but only activates them partially and not to the same extent as full opioid agonists like heroin or methadone. If Buvidal is administered when a person still has full opioid agonists in their system, it will knock those opioids from the receptors, without fully reactivating them. This drop in opioid effect can precipitate withdrawal and make patients feel seriously unwell.

It was recognised that it is often the fear of withdrawal that locks people into heroin using lifestyles and in recognition of this, there were calls among stakeholders and patients that morning appointments were a necessity to avoid the onset of painful withdrawal symptoms, risking a return to illicit opioid use. Relatedly, while some stakeholders discussed running early morning clinics, others called for evening or weekend clinics to allow those in employment to attend without having to take time off or inform their employers.

As noted in Chapter 4, the Bernese method of microdosing buprenorphine alongside methadone to enable faster and less disruptive transitions onto Buvidal was identified as another strategy for improving the process of initiation.

8.8. Peer support

The importance of offering peer support to Buvidal patients was recognised by patients and stakeholders. Indeed, the positive feedback we received about the focus group sessions where patients had the opportunity (sometimes the first they had ever had) to discuss their experiences with fellow patients, demonstrated how useful peer support could be. A key benefit was described in terms of having someone who understands them and their drug-using lifestyle. However, it was also recognised that peer involvement had other benefits, including helping spread the message about Buvidal and encouraging potential patients to enter treatment, as well as guiding them in how to exit.

It was recognised that peer groups offered a safe space for patients to feel comfortable enough to ask questions they would not normally ask of professionals. Peers were also useful in helping patients relax during the assessment process, which was described in unfavourable terms by some patients. Furthermore, interaction with peers helped to demonstrate recovery is possible and death not inevitable.

The participants of one focus group suggested that peer support groups should be offered as part of the treatment package. These patients were of the view that attending such groups (which were described as being distinct from Twelve Step programmes, such as Narcotics Anonymous) should be mandatory to sift out those not ready to stop using heroin and to focus resources on those who were committed to engaging. The value of lived experience in guiding service design was also recognised by stakeholders, including one who recommended peer involvement (in partnership with practitioners) in the allocation of resources.

8.9. Professional support

8.9.1. Psychological support

There was broad agreement among participants that providing Buvidal medication alone to patients is not sufficient and that psychological support (delivered by trained professionals) should also be available to those in need in all parts of Wales. Even in those areas where psychological support was reported to be on offer, it was sometimes in short supply, with patients struggling on long waiting lists. The lack of additional counselling or psychological, therapeutic support was described as the 'number one disadvantage of Buvidal' in terms of its current delivery. This was felt to be particularly important and problematic given the resurfacing of past trauma reported by many Buvidal patients. The lack of capacity to address unmasked trauma through psychological support was also reported in the prison context. The clear recommendation from across participants was that psychological support should go hand-in-glove with the medication throughout the treatment journey.

It was recommended that the provision of psychological support be delivered through a tiered approach (rather than a one-size-fits-all) to maximise effectiveness and ensure all needs are met. In practice, this would resemble a pyramid structure with the provision of a large amount of low-level support and a smaller amount of more specialised in-depth support to those with greater needs. The Buvidal Psychological Support Service[7] (BPSS) in Cardiff and the Vale is an exemplar of this delivery model. It was understood that psychological support could help address the increase in on-top use of other substances (e.g., crack and alcohol) noted among some Buvidal patients. Importantly, it was recognised that to date, services have tended to prioritise opioids and alcohol and that Buvidal has highlighted the need to broaden their work to support patients with other drug problems.

It was also recommended that services capitalise on the clarity of mind reported by many patients to help them move on in their recovery, rather than holding them within a treatment system that requires daily pick-ups of methadone and oral buprenorphine. Importantly, there was a sense the provision of psychological support should be available to patients across the board and not only Buvidal patients. While the costs of providing such support were acknowledged, it was suggested they could be offset by the health and criminal justice savings that it generated.

8.9.2. Psychosocial support

In addition to the provision of psychological support, there was also overwhelming agreement among participants of the need for Buvidal services to include psychosocial support opportunities alongside the medication. Gwent Drug and Alcohol Service's Peer Academy was noted as an exemplar in this regard. The main rationale for this is that patients on Buvidal find themselves with a significant amount of 'freedom' and spare time on their hands, which can lead to boredom and subsequent relapse. The value of occupation and routine in our lives was highlighted, with the recommendation that patients starting Buvidal should be advised to

[7] An evaluation of the BPSS has recently been completed by members of this evaluation team.

consider how not using opioids will affect their ability to do the things in life that they want, need, and are expected to do.

It was suggested that the psychosocial support provided should be individualised. It did not always need to be extensive and that even a number to call would help fill the void between their monthly appointments. Other suggestions included encouraging and supporting patients to go to a prevention group, go for a walk, or join an arts and crafts club, as frequent access to such activities could help people cope with the huge life changes associated with stopping a lifelong habit. One stakeholder described psychosocial activities as the motivational hook that helps people stop using substances. As such, it was viewed as a critical part of the treatment package to support progress and help with reintegration back into local communities, which would in turn help sustain positive treatment outcomes.

As with psychological support, stakeholders believed psychosocial support could offer value for money and help to relieve the societal burden of crime, imprisonment, street injecting, and the spread of blood borne viruses. The opportunity to engage in psychosocial programmes to develop recovery capital while having access to trauma-influenced support and therapy was identified as the building block of a first class Buvidal service.

8.9.3. Check-in support

In addition to the more comprehensive and intensive forms of support outlined above, patients and stakeholders also saw value in having regular check-ins with patients to keep in touch and discuss any emerging issues. It was suggested that check-ins were particularly important at the start of treatment and in the days and weeks following the first injection. Stakeholders also recognised the value of regular check-ins with patients, albeit sometimes from a different service-level perspective (e.g., as an incentive to encourage continued compliance and engagement with treatment).

8.10. Raising awareness and improving understanding of Buvidal

Patients on Buvidal spoke very positively about their experiences and were keen for other people with opioid problems to benefit from the treatment. Word of Buvidal and its positive impact has spread widely through peer-to-peer contact, although this method of awareness raising only works among those in touch with knowledgeable networks. An alternative method suggested in one focus group was hosting ‘Buvidal days’ and handing out fliers to help spread the word of Buvidal as a treatment option. While raising awareness generally was viewed as important, patients also believed more information (‘written very simply in layman’s terms’) needed to be provided on what Buvidal is and how it might affect them.

The need to ensure that health and social care professionals are properly informed about Buvidal was identified by some patients and stakeholders who reported incidents where hospital doctors had no knowledge of Buvidal. The main concern reported by patients and stakeholders was that if doctors are unaware of Buvidal and the possibility that higher doses or different combinations of pain relief might be needed for Buvidal patients, then sufficient pain relief may not be given in the event of an accident. Some patients in one area referred to a ‘Buvidal card’ that provided information about their Buvidal status (a bit like an allergy warning card). This was recognised as potentially useful and there were concerns that these cards, which had once been issued routinely, were now only available on request.

8.11. Developing best practice

In our discussions with stakeholders, two key recommendations were offered for ensuring the provision of high-quality treatment for patients. The first emerged out of concerns that some staff members are not appropriately trained to deliver specialist substance use services and involved the idea of introducing minimum occupational standards.

The second emerged from concerns that staff are working in silos meaning opportunities to share experiences (both good and bad) are being missed. To address this, it was suggested that a community of professional practice be developed through which professionals could learn from one another. It was recognised this would help bring together different strands of work and would be something professionals would make time to attend to enhance their understanding and make useful contacts.

9. Conclusions and recommendations

- The Buvidal evaluation involved extensive pan-Wales consultation with a broad range of stakeholders working in a variety of disciplines and with groups of patients with mixed backgrounds and treatment histories.
- The urgency of the COVID-19 pandemic created a unique opportunity for the rapid roll out of Buvidal across Wales. This led to innovation and widespread uptake, but the speed of implementation inevitably resulted in significant variations across areas in terms of funding, availability and delivery.
- There was widespread support for the continuation of Buvidal in Wales. It was widely believed that Buvidal outperforms methadone and oral buprenorphine across a range of domains and therefore represents good value for money.
- The primary benefits of Buvidal include the freedom it offers from daily attendance at clinics, the slow and steady release of buprenorphine over time, and its blocker action that discourages on-top opioid use.
- Stakeholders and patients were in agreement that the Buvidal injection should be part of a broader package of care that includes access to professional psychological support and meaningful psychosocial activities.
- There was broad acceptance that Buvidal is not for everyone and that it should be an option rather than the only option available to patients.
- Initially hailed as a 'game changer', Buvidal quickly gained popularity. Over time it has become recognised not as a cure-all or silver bullet, but as one important element of a broader treatment framework.
- A series of recommendations for policy, practice and future research emerged from the evaluation, the most important of which is that Buvidal continues to be available as a form of OST and that it becomes a treatment option for all those with clinical need in community and prison settings in all parts of Wales.

In this final chapter we reflect on the findings of the evaluation as a whole and draw some conclusions regarding the rapid roll out and implementation of Buvidal in Wales. We end the chapter and report with a set of recommendations that will help to optimise the efficiency and effectiveness of Buvidal treatment.

9.1. Conclusions

This evaluation of Buvidal has been challenging, complex, and time-consuming, but also rewarding, illuminating, and at times, moving. It has involved extensive pan-Wales consultation with a broad range of stakeholders working in a variety of disciplines and with groups of patients with mixed backgrounds and treatment histories. This has enabled us to develop an in-depth understanding of the evolution of Buvidal treatment in Wales dating back to 2019.

The urgency of the COVID-19 pandemic and the need to limit the spread of the virus created a unique opportunity for the rapid roll out of Buvidal across Wales. While this led to innovation and widespread uptake, the speed at which it was implemented inevitably resulted in significant variations across areas in terms of funding arrangements, availability and delivery.

Despite these differences, all but one participant[8] was in favour of Buvidal continuing in Wales, and there were serious concerns over what might happen if it was stopped. Stakeholders were impressed by the positive outcomes they had witnessed among patients across a variety of domains, many of which align with those reported in other evaluations of long-acting injectable buprenorphine. Many were convinced that it outperformed methadone and oral buprenorphine and therefore offered better value for money, a view that has been confirmed by our analysis of healthcare usage using data from the SAIL databank.

The primary benefits of Buvidal include the freedom it offers in terms of monthly rather than daily attendance at clinics, which can enable patients to live more 'normal' lives and put distance between them and their former drug-using networks (see also Allen et al., 2023; Matheson et al., 2022; Parkin et al., 2023). An additional benefit is the slow and steady release of buprenorphine which reduces (and in some cases stops) withdrawal symptoms and cravings, both of which are key factors in motivating the continued use of illicit opioids (see also Johnson et al., 2022; Neale et al., 2023). Its blocker status is another benefit that helps motivate patients to become, and/or remain, abstinent from on-top opioid use. Buvidal was associated with a range of other health and social outcomes including its potential to reduce (but not eliminate) the risk of opioid overdose.

Many findings from this evaluation align with those found in the literature, such as the reduced risk of overdose (Lee et al., 2021), decreased opioid use (Marsden et al., 2023), and improved quality of life among patients (Montgomery et al., 2025). While quantitative studies suggest the use of other illicit substances may decrease (Marsden et al., 2023), there is qualitative evidence suggesting use of other substances can occur among LAIB patients (Neale and Strang, 2024; Johnson et al., 2022), a finding also reported above in the impact evaluation (e.g., crack use). Positive employment-related outcomes were also similar to those found in the previously published qualitative literature (Parkin et al., 2023a; Gendera et al., 2025).

However, while the interview and focus group findings reported here suggest retention rates were better among Buvidal patients, the current quantitative evidence appears to be mixed, with LAIB retention rates better in the short term (Lintzeris et al., 2021a; Lofwall et al., 2018). Previously published literature also highlighted the strong benefit of LAIB to mental health (Marsden et al., 2023; Montgomery et al., 2025), and while many patients and stakeholders discussed benefits, drawbacks were also mentioned (e.g., unmasking trauma). Lastly, while a lack of withdrawal symptoms and cravings were also frequently reported by patients and stakeholders, the findings from the systematic review of the previously published literature suggest that the relationship between LAIB and these constructs is complicated (Lintzeris et al., 2021a; Lofwall et al., 2018; Clay and Duff, 2024).

Alongside the widespread support for the continuation of Buvidal in Wales there was also widespread acceptance that Buvidal is not for everyone and that it should be an option rather than the option for patients with opioid problems. This view was grounded in a number of considerations. First, some patients are not yet ready (or do not want) to stop using opioids entirely but nevertheless wish to be in treatment for the important harm reduction benefits it provides. Second, some patients are not yet ready to address the underlying trauma that their opioid use has been helping them to manage. Third, some patients struggle with the lifestyle

[8] More than 200 people took part in the evaluation. The one dissenting voice was a stakeholder who completed the survey.

changes that come with monthly rather than daily attendance at clinics or pharmacies. Finally, there is a small group of patients who experience unexpected effects from Buvidal, including withdrawal symptoms despite increasing doses. For these groups of patients, maintaining access to methadone and oral buprenorphine is clinically and ethically important.

Maintaining access to Buvidal is also important. In the absence of additional ring-fenced funding for the Buvidal injections, services would need to use their existing budgets to pay for this on top of the other existing costs associated with treatment. The impact of this on services would be significant and could affect staff (who might lose their jobs to free up treatment spaces) and patients (who might be transferred to other forms of OST). The benefits of Buvidal for patients, as well as for communities and prisons, may end up being limited to areas with sufficient funds to pay for treatment, thereby creating a postcode lottery of availability. Any reduction in the funding for Buvidal would likely necessitate difficult choices to be made regarding which patients should be prioritised. Inequity already exists in the system (e.g. patients across Wales do not have an equal chance of accessing Buvidal and not all patients can access Buvidal through GP shared care schemes), but it would be significantly worsened in this situation.

While stakeholders recognised the cost implications, it was nevertheless recommended that to maximise the effectiveness of Buvidal, investment in the provision of psychological support for patients (to address underlying trauma) and meaningful psychosocial activities (to fill their days) was needed (see also Lancaster et al., 2022; Parkin et al., 2023a; Parsons et al., 2020). Importantly, psychological support delivered by qualified staff and access to psychosocial activities was thought to be necessary for all patients in substance misuse services, rather than limited to Buvidal. The costs, it was argued, would be more than offset by the savings made to the NHS and criminal justice system through the delivery of more effective treatments. This argument is supported by the findings of our systematic review of the literature (see Chapter 3) as well as our analysis of healthcare service usage using data from the SAIL databank (see Chapter 6).

In relation to the latter, our analysis has shed some light on how patients on different forms of OST differ in terms of their use of healthcare services. Setting the data quality issues aside, the analysis showed patients receiving Buvidal were less likely than those on methadone and oral buprenorphine to use the ambulance service and attend emergency departments. Drawing on insights from the wider evaluation, this finding might reflect lower levels of on-top opioid use among Buvidal patients, which reduces the risk of overdose. It is also possible that Buvidal contributes to greater overall stability, making patients less likely than those on other forms of OST to experience accidents, injuries or crises that require emergency care.

Buvidal patients were also less likely than methadone patients to be hospitalised in general and less likely than those on oral buprenorphine to have elective hospitalisations. They were also less likely than patients on other forms of OST to attend GP appointments. These findings may be because patients on Buvidal are better able to address their healthcare needs through outpatient care, which allows conditions to be managed without hospital admission. Alternatively, it might be because they are experiencing better general health, possibly due to improved self-care, diet and more exercise, leading to fewer issues that require hospitalisation or GP attention.

While it was not possible to compare the risk of death between the different types of treatment due to confounding factors (e.g. spill-over effects of other treatment types and unknown underlying health conditions), we were able to compare the number of deaths from all causes and the number of deaths related to drug poisoning recorded during the study period (April 2020 to August 2024). The analysis showed that more than half of the deaths recorded were among patients on methadone while the remainder were fairly evenly split across patients on Buvidal and patients on oral buprenorphine. This pattern might be explained through pharmacology-related factors. Methadone as a full agonist carries a higher risk of respiratory depression and more easily allows for 'on top' opioid use whereas buprenorphine is a partial agonist that provides greater protection against overdose. It might also be explained through patient-level factors. Patients on methadone may have more complex health and social histories than those on Buvidal or oral buprenorphine, which puts them at greater risk of dying. Without knowing the cause of death, it is difficult to draw any firm conclusions. What is clear, however, is that some patients on Buvidal do die and in some cases, this is a result of drug poisoning.

Looking ahead to the future, GP shared care schemes appear to be an important part of the Buvidal jigsaw in providing a pathway into the community for more stable patients, thereby releasing capacity within specialist substance misuses services to take on new and less stable patients. Involving GPs also provides an opportunity for patients to address their wider health problems and for supporting reintegration into their local communities, benefits that are already highlighted in the UK guidelines on clinical management of drug misuse and dependence (The Orange Book, 2017). There is also potential for community pharmacies to play a role in the delivery of Buvidal, although given the capacity issue highlighted by stakeholders, this is likely to require a shared care arrangement to ensure that effective monitoring and support is provided to patients.

At the time of writing, Buvidal is being used in Wales primarily as a form of maintenance treatment with no restrictions imposed on the duration of treatment. However, the success of some patients in coming off Buvidal, some without even intending to, suggests it could be used more widely as a detoxification pathway. Early experiences suggest this works best when patients are confident of a swift and simple route back into treatment if necessary, and where routine follow-ups are continued for many months after their final dose. Further research is necessary to explore and confirm Buvidal's effectiveness in this regard.

Initially hailed as a 'game changer', Buvidal quickly gained popularity. Over time, however, it is now recognised not as a cure-all, but as one important element of a broader treatment framework.

9.2. Recommendations

In light of the reflections described above, in this final section we offer a series of recommendations to help guide the future of Buvidal treatment in Wales. The text in Table 9 presents the main recommendations that have emerged from the evaluation. Below the table, we present a more detailed set of recommendations, which, for clarity, we have separated into recommendations for policy, practice and future research.

Table 9.1 Summary of main recommendations

1. Buvidal continues to be available as a form of OST in Wales.
2. Buvidal becomes a treatment option for all patients with clinical need in community and prison settings in all parts of Wales.
3. Professional psychological support and meaningful psychosocial activities are made available to all OST patients in Wales.
4. Patients are informed that the risk of overdose with strong or large quantities of opioids remains a possibility while on Buvidal and issued with naloxone kits.
5. GP shared care services are further developed and expanded across Wales and the possibility of developing CP (Community Pharmacy) shared care services for Buvidal is explored.
6. Peer (patient) networks and forums are further developed and expanded across Wales to enable patients to share experiences of Buvidal and support one another.
7. A community of professional practice is established bringing together stakeholders from across Wales to share lessons and best practice regarding Buvidal treatment.
8. Data collection practices are strengthened to minimise errors and omissions in the Substance Misuse Database.
9. Future research examines the clinical outcomes of Buvidal patients focusing on the likelihood of substance switching and improving engagement with services.

9.2.1. Recommendations for policy

We recommend that Welsh Government works with partners to:

- Continue and expand the availability of Buvidal as a treatment option to all those with a clinical need in Wales, including patients in community and prison settings.
- Expand the provision of professional psychological support and meaningful psychosocial activities for patients on all forms of OST across all parts of Wales.
- Distribute funding for Buvidal equitably across Wales using up-to-date assessments of clinical need and demand.
- Increase the ring-fenced budget for Buvidal to cover: the costs of the medication, the costs of complying with regulations over the storage, transport and administration of a Schedule 3 drug, and the costs of providing adequate professional psychological and psychosocial support for patients.
- Continue the development of GP Shared Care services and the integration of Buvidal within these services across all parts of Wales to release capacity in specialist substance misuse services and support community reintegration.

- Explore the use of Community Pharmacy (CP) Shared Care services for the delivery of Buvidal.
- Conduct an independent national review of substance misuse treatment services across Wales to assess current levels and quality of provision of psychological and psychosocial support.
- Develop minimum occupational standards for staff working within substance misuse services.
- Review OST provision in Welsh prisons, in line with Dame Carol Black's recent review of prisons, to ensure equity of access to the full range of OST options in closed and open establishments[9].
- Discuss with the UK Government the rescheduling of Buvidal under the Misuse of Drugs Act Regulations 2001 based on the limited opportunities for its misuse and diversion.
- Discuss pricing options with representatives of the manufacturer of Buvidal and explores opportunities for the development of alternative long-acting formulations of buprenorphine with other pharmaceutical companies.
- Develop guidelines for the less painful administration of Buvidal.
- Create and disseminate learning materials about Buvidal to educate health and social care practitioners more broadly about appropriate pain relief for Buvidal patients.

9.2.2. Recommendations for practice

We recommend that APBs and staff working in community and prison-based substance misuse services work together with partners to:

- Develop a community of professional practice within which best practice can be shared and lessons learned. This could help to ensure more consistency across areas in terms of the day-to-day delivery of Buvidal (e.g., initiation processes and policies for restarting patients who have missed doses).
- Develop and/or utilise existing local and national peer networks and forums where patients can share their experiences and learn from one another.
- Strengthen and develop robust data recording practices to minimise missing and inaccurate entries within the Substance Misuse Database, facilitating more accurate economic assessments and reducing the need to make assumptions.
- Ensure that Buvidal patients are advised that overdose is still possible with strong opioids such as fentanyl and nitazenes or with large quantities of opioids and provided with naloxone kits.
- Ensure service-level specifications include provision for appropriate psychological support and access to structured psychosocial activities to meet the diverse needs of all patients on OST.

9.2.3. Recommendations for future research

We will be undertaking further analyses of the SAIL databank to explore criminal justice outcomes and employment, training and education outcomes among patients on different

[9] This recommendation aligns with that of Dame Carol Black (2024) in the internal review of drug treatment in prisons in England.

forms of OST (see the Analysis of healthcare activities and associated costs report). In addition to this work, we recommend that researchers with an interest in Buvidal and other forms of OST examine:

- Alternatives to Buvidal: this might include the different use of oral buprenorphine to mimic the effects of Buvidal (e.g., with larger and/or more frequent oral doses; reducing opportunities for misuse and diversion)
- Cost-effectiveness of Buvidal: this might include quality of life analyses comparing treatment groups in terms of cost per quality adjusted life year and analyses of productivity loss per patient using average earnings and employment rates. These analyses were beyond the scope of the current evaluation, which used SAIL data to compare healthcare service usage and associated costs among OST groups.
- Substance switching among Buvidal patients: this would involve identifying the characteristics of patients who are most at risk of starting or increasing their use of other substances while on Buvidal.
- Access to Buvidal: current findings suggested that, in Wales, there are disparities in terms of possibility of accessing a Buvidal prescribing, both in the community and in prisons. Although several factors may be at play in explaining, at least in part, these differences, more educational and research work needs to be carried out to better address these gaps in accessing treatment.
- Pharmacokinetics and pharmacodynamics of Buvidal: some findings of the current study suggested there may be differences in both pharmacokinetics and pharmacodynamics of Buvidal/LAIBs compared with oral buprenorphine. However, there is a lack of consensus surrounding these differences and more research is needed. Future studies have potential to inform our understanding of the mechanism of action of LAIB preparations and the onward development of treatment regimens, dosing schedules, patient selection processes and response prediction
- Long-term follow-up: current findings from our analysis of the SAIL databank show that a small number of patients drop out of Buvidal treatment. Research is needed to explore the reasons for drop-out as well as the reasons for re-engagement in either Buvidal or other forms of OST. Research is also needed to improve understanding of broader life changes among Buvidal patients over longer periods than have been examined to date.
- Detoxification pathway: findings from the current study suggest that Buvidal could be a useful detoxification tool, but the evidence base supporting this is slim. Research is needed to evaluate the effectiveness of Buvidal as a tool for detoxification.
- Social media analysis: our review of the literature identified social media analysis as a useful tool for exploring the experiences of a large number of patients receiving LAIB. Social media posts could therefore be reviewed to assess mentions of specific phenomena such as withdrawal, cravings, cognitions, anxiety, insomnia, detoxification.
- Based on the findings of our analysis of the SAIL data (e.g. the higher number of deaths among patients on methadone and the similar number of deaths among patients on oral buprenorphine and Buvidal), we recommend that any future evaluations of Buvidal include two distinct comparison groups. This will help to ensure that the outcomes of patients on oral buprenorphine are not confounded by those of patients on methadone.

10. Annex

Figure 3.1 Effect direction plot - RCTs

Study	Study Design	Retention (LT)	Retention (ST)	Abstinence - Opioids (LT)	Abstinence - Opioids (ST)	Overdose (LT)	Overdose (ST)
Lee et al. (2021)	RCET		▲		▲		◄►
Lintzeris et al. (2021)	RCT	▼		▼		▲	
Lofwall et al. (2018)	RCT	▼	▲	▲	▲	▲	
Marsden et al. (2023)	RCT	▲		▲	▲	▲	

LEGEND
Study design: RCT: Randomised Controlled Trial; RCET: Randomised Comparative Effectiveness Trial
Long term (LT); Short term (ST)
Effect direction: upward arrow ▲= positive health impact, downward arrow ▼= negative health impact, sideways arrow ◄►= no change/mixed effects/conflicting findings
Sample size: Final sample size (individuals) in intervention group; large arrow ▲ >300; medium arrow ▲ 50-300; small arrow ▲ <50

Figure 3.2 Effect direction plot - RCTs

Study	Study Design	Mental health (LT)	Mental health (ST)	Quality of Life (LT)	Quality of Life (ST)	Withdrawal (LT)	Withdrawal (ST)	Cravings (LT)	Cravings (ST)
Lee et al. (2021)	RCET								
Lintzeris et al. (2021)	RCT	▲	▲	▲	▲	▼	▲	▼	▲
Lofwall et al. (2018)	RCT					◄►	◄►	◄►	◄►
Marsden et al. (2023)	RCT	▲		▲	▲			▲	

LEGEND
Study design: RCT: Randomised Controlled Trial; RCET: Randomised Comparative Effectiveness Trial
Long term (LT); Short term (ST)
Effect direction: upward arrow ▲= positive health impact, downward arrow ▼= negative health impact, sideways arrow ◄►= no change/mixed effects/conflicting findings
Sample size: Final sample size (individuals) in intervention group Large arrow ▲ >300; medium arrow ▲ 50-300; small arrow ▲ <50

Figure 3.3 Effect direction plot - NRSI

Study	Study Design	Retention	Abstinence - Opioids	Overdose	Mental health	Quality of Life	Withdrawal	Cravings	Abstinence (all combined)
Frost et al. (2019)	OB		▲				▲	▲	
Guillery et al. (2023)	OB						◄►	▼	▼
Hard & DeSilva (2023)	Pilot				▲				
Lee et al. (2023) - Methadone comparator	MR	▼	▲	▲					▲
Lee et al. (2023) - Oral bup comparator	MR	▲	▼	▲					▼
Lintzeris et al. (2021b) - Methadone comparator	MR								▲
Lintzeris et al. (2021b) - Oral bup comparator	MR								▲
Milo (2025)	MR	▲	▲	◄►					
Montgomery (2025)	MR		▲		▲	▲			

LEGEND
Study design: OB: Observational: MR: Medical Records Review
Long term (LT); Short term (ST); Oral bup = Oral buprenorphine
Effect direction: upward arrow ▲= positive XR impact, downward arrow ▼= negative XR impact, sideways arrow ◄►= no change/mixed effects/conflicting findings
Sample size: Final sample size (individuals) in intervention group Large arrow ▲ >300; medium arrow ▲ 50-300; small arrow ▲ <50

Figure 4.1 An infographic summarising findings from the process evaluation

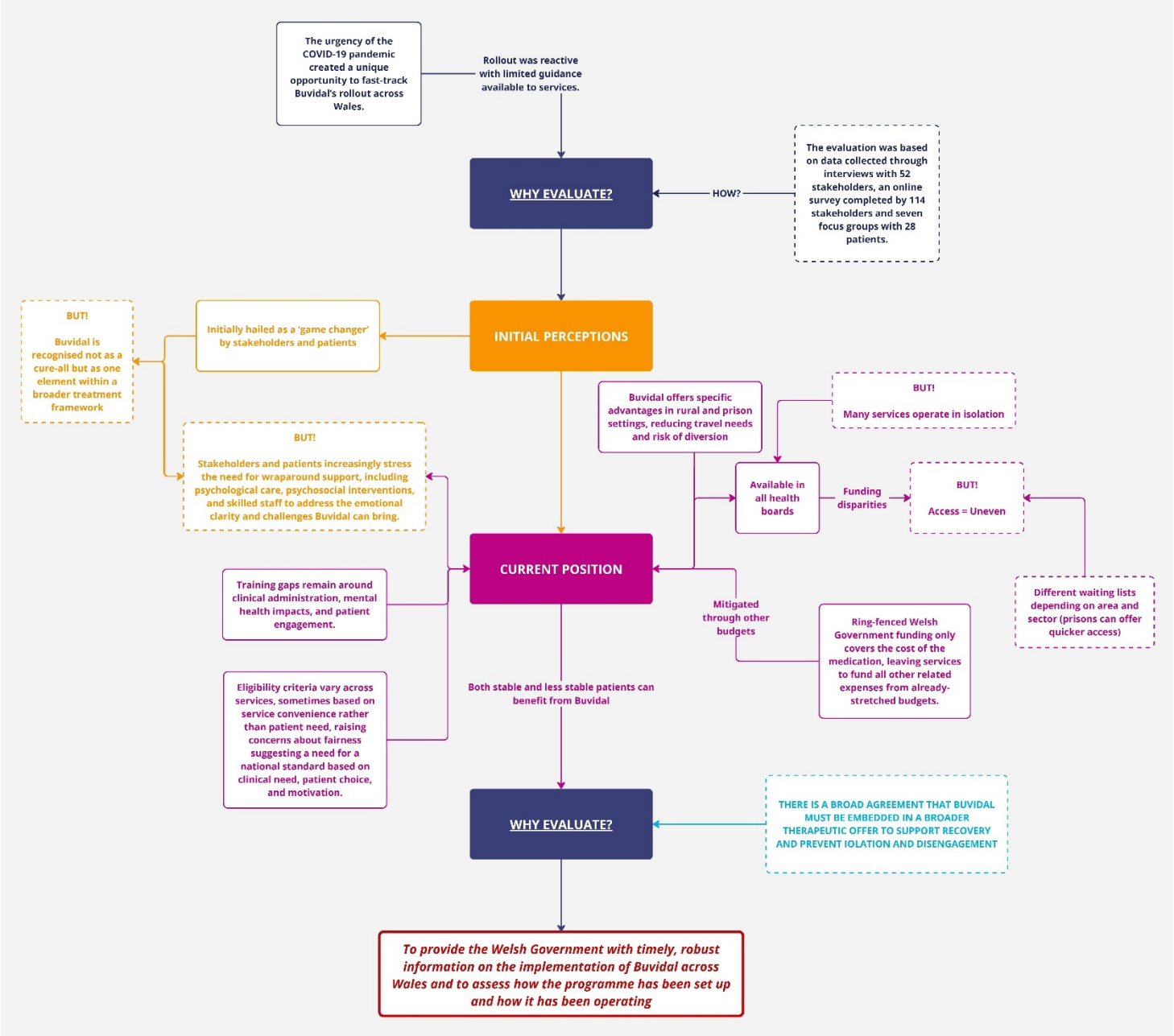

Figure 5.1 An infographic summarising findings from the impact evaluation

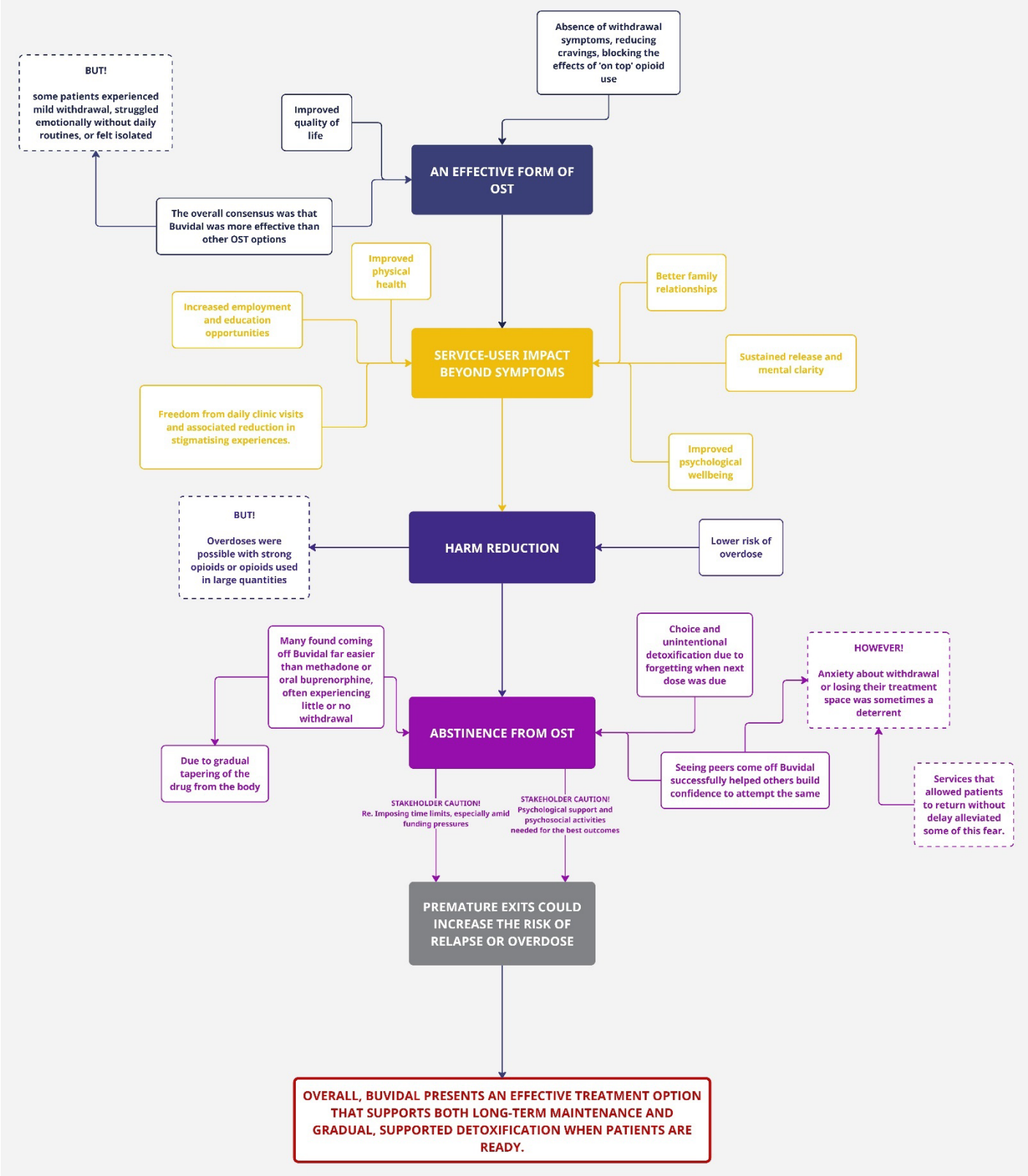

Figure 7.1 Buvidal Theories of Change

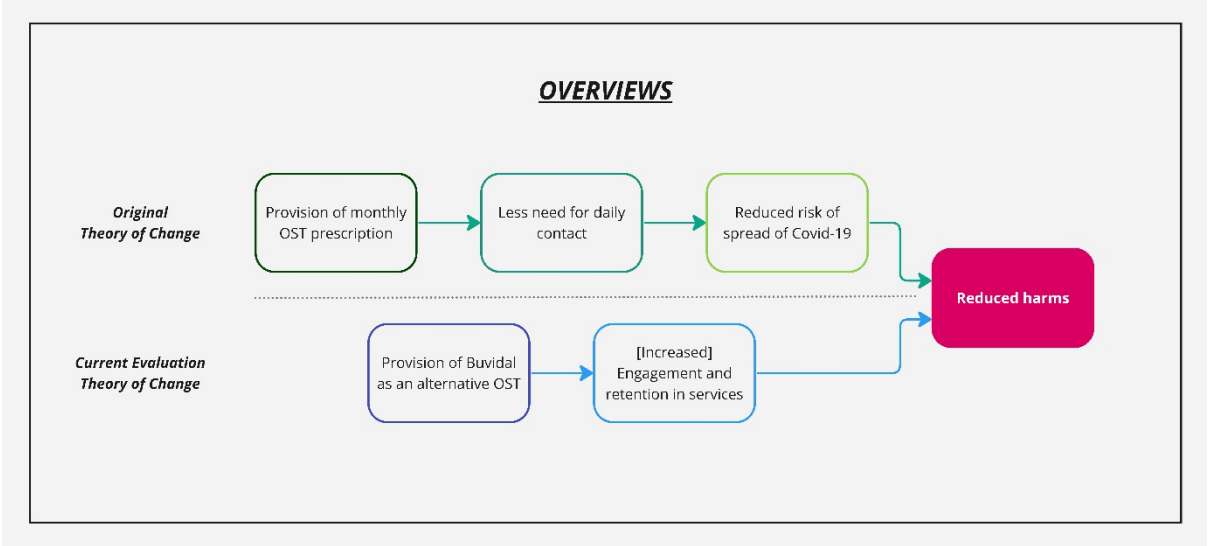

Figure 7.2 Final simplified logic model

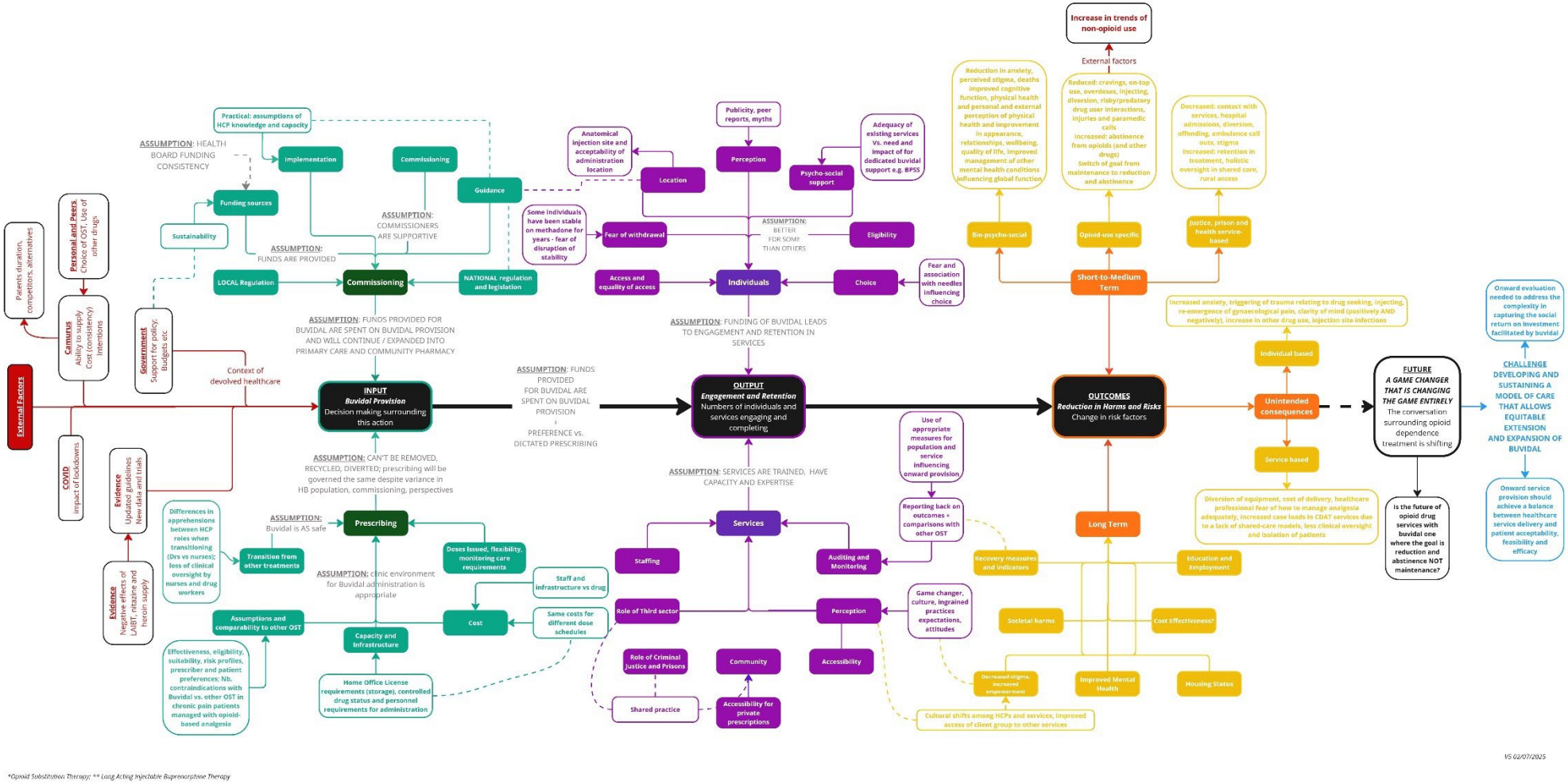

Figure 8.1 Proposed future delivery model for Buvidal