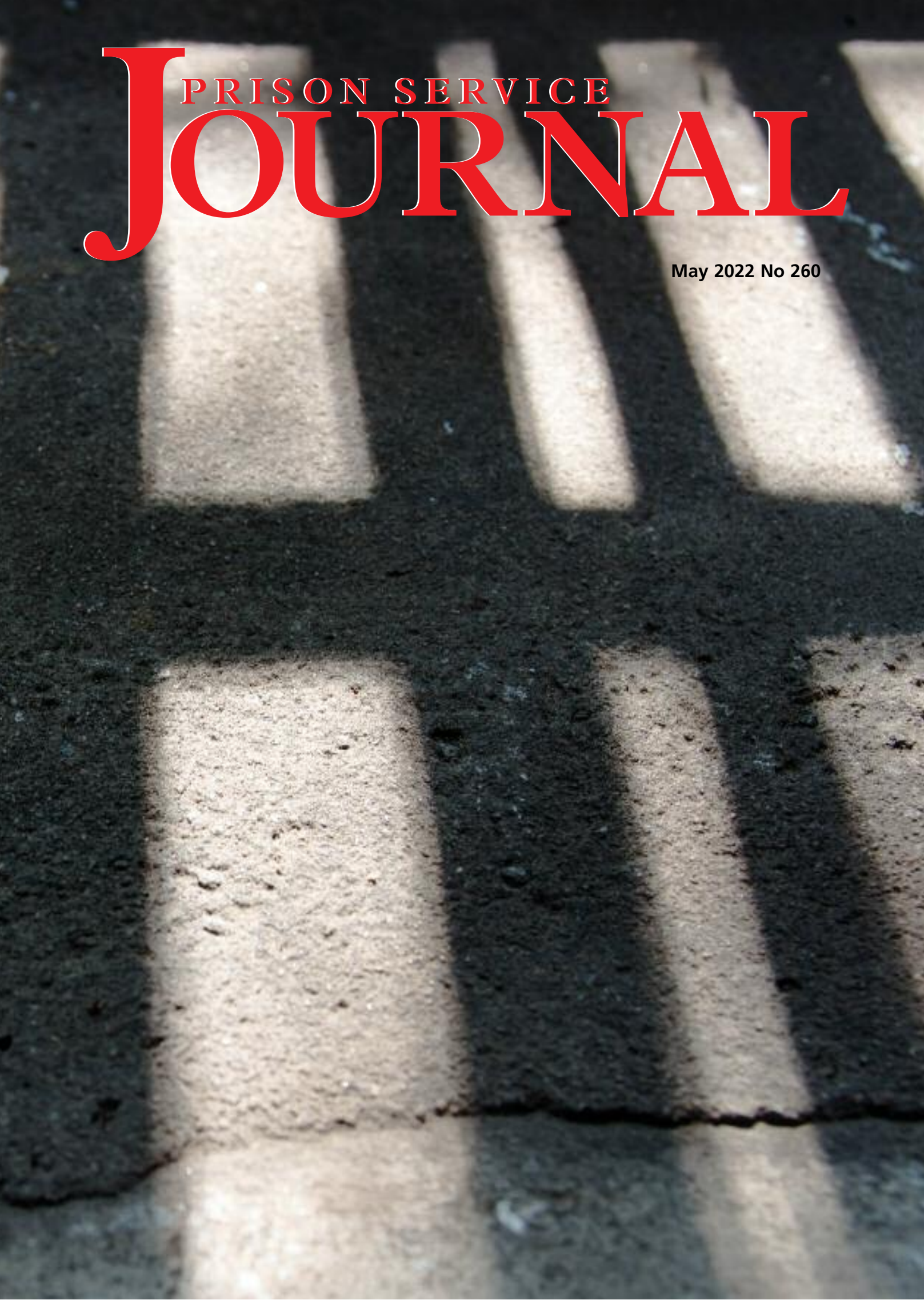

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# Impact of introducing an alternative buprenorphine formulation on opioid substitution therapy supervision within UK prison settings

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## Background

**Opioid substitution therapy (OST) involves the prescribing and administration of pharmaceutical opioids for the treatment of dependence. OST is designed to reduce illicit opioid use and drug-related harms, reduce and prevent withdrawal symptoms, promote changes in lifestyle, and ultimately abstinence where this is an attainable outcome[1].**

The National Drug Treatment Monitoring System estimated that there were 140,599 adults in England who were in contact with drug and alcohol treatment services for opiate dependency in 2019—2020[2]; of these, approximately 1 in 5 were in a prison setting[3]. The most commonly prescribed opioids used for OST in prisons are methadone and buprenorphine. However, buprenorphine sublingual tablets (whole or broken into granules) can take between 5 to 10 minutes to dissolve, providing opportunities for diversion of prescribed buprenorphine in prison settings[4]. Historically, this has meant that the offer of buprenorphine has been discouraged or limited in UK prisons. This impacts on both equivalence and continuity of care versus the community offering.

Where buprenorphine is not a standard offering in prison, patients entering these establishments have the option to move to methadone maintenance or undergo detoxification; both options are suboptimal and not always the best choice for the patient. For prisons that offer buprenorphine for OST, the current process for supervision of buprenorphine administration can be challenging for the staff involved and for patients and can lead to confrontation.

Buprenorphine oral lyophilisate (Espranor®) is an innovative form of buprenorphine that is designed to rapidly disperse on the tongue. One study found 96.3 per cent of buprenorphine oral lyophilisate administrations achieved partial disintegration on the tongue in ≤15 seconds, with over 58.0 per cent of administrations completely dissolving within 2 minutes[9]. By comparison, only 71.8 per cent of sublingual buprenorphine administrations achieved partial disintegration in ≤15 seconds and 5.1 per cent completely dissolved within 2 minutes, with a median time of 10 minutes for the tablets to completely dissolve.[8,9]

Evidence on the impact of switching to buprenorphine oral lyophilisate from buprenorphine

1. National Institute for Health and Care Excellence. (2007) *Methadone and buprenorphine for the management of opioid dependence* (TA114). Available at: https://www.nice.org.uk/guidance/ta114 (Accessed: 2 July 2021).
2. Public Health England. (2020) *Substance misuse treatment for adults: statistics 2019 to 2020*. Available at: https://www.gov.uk/government/statistics/substance-misuse-treatment-for-adults-statistics-2019-to-2020 (Accessed: 2 July 2021).
3. Public Health England. (2021) *Substance misuse treatment in secure settings: statistics 2019 to 2020.* Available at: https://www.gov.uk/government/statistics/substance-misuse-treatment-in-secure-settings-2019-to-2020 (Accessed: 2 July 2021).
4. European Medicines Compendium. (2021) *Buprenorphine 8mg Sublingual Tablets Summary of Product Characteristics*. Available at: https://www.medicines.org.uk/emc/product/4163/smpc (Accessed: 17 September 2021).
5. Reimer, J. et al. (2016) 'The Impact of Misuse and Diversion of Opioid Substitution Treatment Medicines: Evidence Review and Expert Consensus', *European Addiction Research*, 22(2), pp. 99–106. Available at: https://www.karger.com/Article/Fulltext/438988 (Accessed: 3 November 2021).
6. Wright, N. et al. (2011) 'Comparison of methadone and buprenorphine for opiate detoxification (LEEDS trial): a randomised controlled trial', *British Journal of General Practice*, 61(593), pp. e772–e780. Available at: https://pubmed.ncbi.nlm.nih.gov/22137413/ (Accessed: 3 November 2021).
7. Wright, N. et al. (2016) 'Addressing misuse and diversion of opioid substitution medication: guidance based on systematic evidence review and real-world experience', *Journal of Public Health*, 38(3): pp. e368–e374. Available at: https://pubmed.ncbi.nlm.nih.gov/26508767/ (Accessed: 3 November 2021).
8. European Medicines Compendium. (2020) *Espranor 8 mg oral lyophilisate Summary of Product Characteristics.* Available at: https://www.medicines.org.uk/emc/product/2317/smpc (Accessed: 2 July 2021).
9. Strang, J. et al. (2017) 'Randomised Comparison of a Novel Buprenorphine Oral Lyophilisate versus Existing Buprenorphine Sublingual Tablets in Opioid-Dependent Patients: A First-in-Patient Phase II Randomised Open Label Safety Study', *European Addiction Research,* 23(2), pp. 61–70. Available at: https://www.karger.com/Article/Abstract/456612 (Accessed: 3 November 2021).

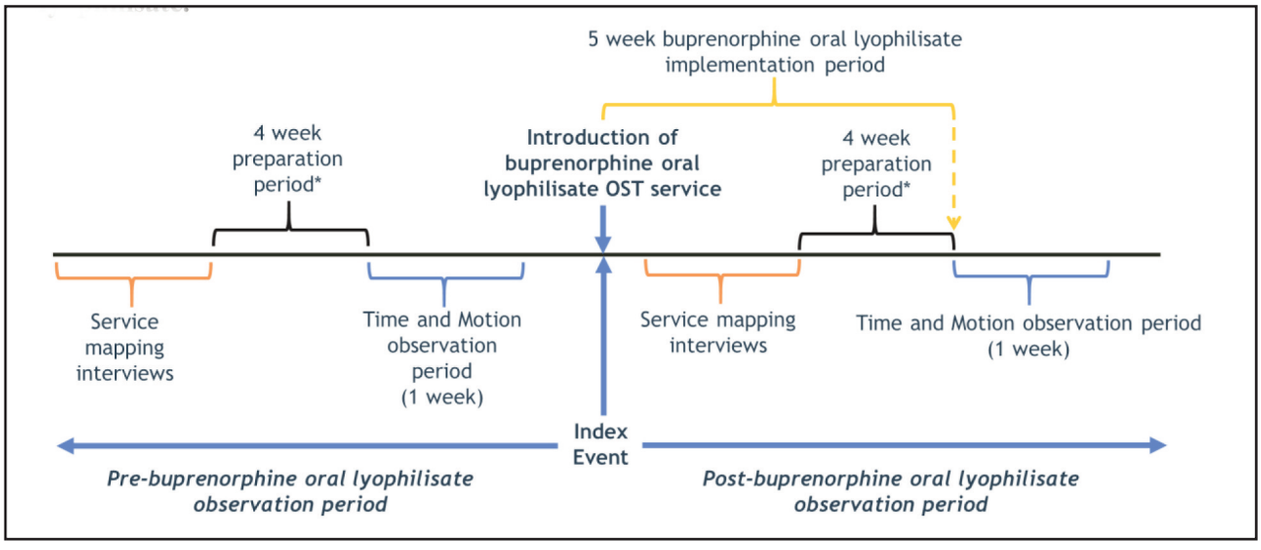
sublingual tablets in the prison setting is lacking. The aim of this study was to assess the benefits of adopting buprenorphine oral lyophilisate on the OST supervision process in two Practice Plus Group prisons. It is hoped that this change in OST service will provide benefits to patients and staff and may also reduce the misuse of OST in this setting.

## Methods

This was a prospective, time and motion study carried out at two UK prisons, HMP Leeds and HMP Pentonville, receiving OST services through Practice Plus Group. The study included two observation periods of one week prior to and one week following the adoption of buprenorphine oral lyophilisate. The time and motion observer was trained prior to the commencement of the study to enable uniform data recording procedures, and attended a minimum of three OST supervision sessions during each observation period. Observers recorded data on specifically designed paper case report forms. The total supervision schedule was then compared between the two observation periods (Figure 1).

**Figure 1. Study design. The study included a time and motion observation periods of one week prior to the adoption to buprenorphine oral lyophilisate and one week following the adoption of buprenorphine oral lyophilisate, with a five week implementation period to enable the Practice Plus Group staff and patients to become familiar with the supervision of buprenorphine oral lyophilisate.**

Patients included in the study were aged 18 years and over and were treated with buprenorphine formulations for




**A period of 4 weeks was allowed between completion of the service mapping interviews and the start of the time and motion observation period, to enable preparation of the time and motion CRF (which was informed by the outcome of the interviews).*

OST (in receipt of a stable dose of buprenorphine for at least 4 days prior to evaluation) in a Practice Plus Group prison during the pre- and/or post-buprenorphine oral lyophilisate observation period. Patients unwilling or unable to provide written informed consent to be observed during OST administration visits were excluded.

The primary endpoint was the time required for supervision of OST administration visits pre- and post-adoption of buprenorphine oral lyophilisate. Secondary endpoints included changes in cost to the OST service, prescribed dose, and patient and staff experiences associated with the change from tablets to buprenorphine oral lyophilisate. To gain a better understanding of patients' and staff experiences of the OST service following the introduction of buprenorphine oral lyophilisate, semi-structured interviews were held by telephone with the first 12 consenting patients and 6—10 nurse/pharmacy technicians across the two participating sites. Patient interviews covered areas related to: perceptions of the OST supervision process, subjective dose equivalence (number of past buprenorphine treatments including maximum dosage), the acceptability of buprenorphine oral lyophilisate and the risks associated with diverted OST medication in prison (number of instances when caught for buprenorphine diversion, drug debts, intimidation and violence) following the introduction of buprenorphine oral lyophilisate. Staff interviews covered areas related to perceived changes in working practice, personal safety and level of confrontation related to OST administration following the introduction of buprenorphine oral lyophilisate.

Comparative statistical analysis and appropriate statistical tests for significance were used. The study was approved by Her Majesty's Prison and Probation Service's National Research Committee.

## Results

### Time and motion

A total of 120 OST administration episodes were observed across the two prison sites; 50 episodes were observed in the pre-buprenorphine oral lyophilisate observation period and 70 episodes in the post-buprenorphine oral lyophilisate observation period.

The overall OST administration time per episode (from presenting identification to when the patient leaves the hatch) was lower in the post-buprenorphine oral lyophilisate observation period (median [IQR] of 2.8 [2.2—3.6] minutes) compared to the pre-buprenorphine oral lyophilisate observation period (median [IQR] of 7.3 [5.9—8.2] minutes, p<0.001). Similarly, other aspects of OST supervision, including time to present identification, time to prepare medication, time to administer medication, supervision time, and time for checking medication had dissolved, were all significantly lower in the post-buprenorphine oral lyophilisate observation period than in the pre-buprenorphine oral lyophilisate observation period (Table 1). Assuming a patient has a daily episode of buprenorphine oral lyophilisate administration over the course of a year, on average, there could be a potential staff cost saving for administration of OST of £514.65 per patient.

**Table 1. Impact of introducing buprenorphine oral lyophilisate on OST supervision.**

| | Pre-buprenorphine oral lyophilisate (n=50) | Post-buprenorphine oral lyophilisate (n=70) | P value* |
|---|---|---|---|
| Overall OST administration time per episode (mins)† | 7.3 (5.9—8.2) | 2.8 (2.2—3.6) | <0.001 |
| Time to present identification (secs) | 11.5 (5.0—30.0) | 5.0 (4.0—20.0) | 0.004 |
| Time to prepare medication (secs) | 47.5 (30.0—78.5) | 30.0 (20.0—46.5) | <0.001 |
| Time to administer medication (secs) | 10.0 (7.0—14.3) | 15.0 (10.0—55.5) | <0.001 |
| Supervision time (mins) | 4.7 (3.5—5.7) | 1.5 (0.8—2.3) | <0.001 |
| Time for checking medication has dissolved (secs) | 8.5 (5.0—15.0) | 4.0 (3.0—10.0) | <0.001 |

All values stated are median (IQR).
*Mann-Whitney Test. †Primary endpoint.
n/a, not available; IQR, interquartile range; OST, opioid substitution therapy.

### Cost

The median (IQR) cost of drug administered per episode was £2.76 (£2.01—£3.92) in the pre-buprenorphine oral lyophilisate observation period vs £1.79 (£1.29—£2.57) in the post-buprenorphine oral lyophilisate observation period. Drug costs were based on those paid by Practice Plus Group at the time of study. There was no change in prescribed dose of buprenorphine per episode between the pre- and post-buprenorphine oral lyophilisate observation periods (median [IQR] 10.0 [6.5—13.5] mg vs 10.0 [8.0—14.0] mg, respectively).

### Patient and staff interviews

Semi-structured interviews with patients and staff indicated that buprenorphine oral lyophilisate resulted in less diversion in comparison to other OSTs. However, patients were able to find ways to conceal and divert buprenorphine oral lyophilisate, something that will require further monitoring. Some staff members stated that it took some time to educate patients in how buprenorphine oral lyophilisate is administered but suggested that the introduction of buprenorphine oral lyophilisate had positively impacted the daily routine and resource management in aspects such as reduced medication queues, which ultimately saved time and prison resources (supplementary table 1 and 2). Some patient and staff quotes on the topic were:

> *Patient quote: 'It [diversion] does happen, but they are not getting as much out whereas before they could get loads out because you spit it out after a few minutes whereas with Espranor® it is just like that. With Espranor® you can't do that so it is a good thing.'*

> *Patient quote: 'No, there is a difference [between buprenorphine oral lyophilisate and sublingual tablets]. I would be lying if I said otherwise. There is a difference. If you are getting bullied for it, you can say, 'Look, I am on the Espranor®, mate. I tried my*

*hardest, but she makes me...' and they have to back off because everybody knows the way it works.'*

*Staff quote: '..with patients trying to conceal it, there's not much they can do about it because it dissolves quicker. Whereas previously when we used to crush them, they used to swap white powder to a paracetamol or another tablet in a different pot, to say that, 'Oh', whereas that doesn't happen now.'*

**Adverse events**

Buprenorphine oral lyophilisate was well tolerated during the study. A total of 7 patients experienced non-serious adverse events during the time and motion study or during interviews. Of these, 2 patients recovered, while 5 patients had not made a full recovery at the time of data collection. The 7 patients' AEs were described as: rash; sleep disturbance, sweating, cramping; vomiting, sleep disturbance, appetite reduction, snappiness; hot flushes, lethargic, blackouts, deteriorating eyesight; pain in knees; diarrhoea, vomiting, appetite loss, sleeplessness; flu-like symptoms.

## Discussion

The current supervision process of buprenorphine in prison settings can be challenging for staff and patients, involve long waiting times, and can lead to confrontation. Recent studies have noted that the routine diversion of opiate substitutes to other prisoners is a key concern[10]. Streamlining administration using new OST formulations — including fast-dissolving buprenorphine oral lyophilisate or long-acting depot style injections — has been highlighted as a positive development[10,11].

This is the first study to evaluate the impact of introducing a new buprenorphine product on OST supervision within a UK prison setting. The results show that the overall time required for OST administration was significantly lower in the post-buprenorphine oral lyophilisate observation period than in the pre-buprenorphine oral lyophilisate observation period. There was also a significant reduction in time spent on supervision of the OST process following the adoption of buprenorphine oral lyophilisate, potentially freeing up time for staff to focus on patient care.

The new supervision regime has the potential to be more patient friendly, less intimidating and providing greater dignity. The change to buprenorphine oral lyophilisate was acceptable to staff, who suggested the positive impact on resource management. Also, both patients and staff agreed that buprenorphine oral lyophilisate resulted in less diversion in comparison to other OSTs.

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The arrival of a rapidly dissolving form of buprenorphine may allow for continuity of care and patients to be offered the same form of OST that they had in the community, avoiding the need for unnecessary detoxes or conversions to methadone. Practice Plus Group have moved the majority of patients across all their prisons to buprenorphine oral lyophilisate. This may allow for more accurate financial forecasting, which could release funds to be redirected to additional services. This may be accompanied by cost savings if buprenorphine oral lyophilisate were more widely rolled out in other prisons.

The study has several limitations. First, participant consent was a requirement of the study, which may have introduced selection bias and result in a study sample that may not be representative of the wider patient population who switch to buprenorphine oral lyophilisate. Second, data obtained from participant-reported outcomes rely on the completeness of the answers provided by participants, which may be subject to reporting bias. Finally, insufficient quantitative data on OST diversion was available to compare incidences of OST diversion before and after introduction of buprenorphine oral lyophilisate treatment.

Despite these limitations, our findings suggest that buprenorphine oral lyophilisate was associated with a significantly lower overall time required for OST

10. Alam, F. et al. (2019) 'Optimising opioid substitution therapy in the prison environment', *International Journal of Prisoner Health*, 15(4), pp. 293–307. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6761913/ (Accessed: 3 November 2021).
11. Neale, J. et al. (2019) 'Prolonged-release opioid agonist therapy: qualitative study exploring patients' views of 1-week, 1-month, and 6-month buprenorphine formulations', *Harm Reduction Journal,* 16(1), pp. 1–9. Available at: https://harmreductionjournal.biomedcentral.com/articles/10.1186/s12954-019-0296-4 (Accessed: 3 November 2021).

administration and time spent on supervision of the OST process in the UK prison setting.

## Conclusion

This change in OST service may provide benefits to patients and staff, including better staff and patient experience of supervision, release of staff capacity due to reduced supervision time, cost savings, and also reductions in the rates of the diversion and misuse of OST in this setting.


## Acknowledgement

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## Supplementary materials

Supplementary material associated with this article can be found in the online version.

**Supplementary material**

**Supplementary table 1. Patient interviews.**

| Theme | Summarised patients' views |
|---|---|
| Acceptability of buprenorphine oral lyophilisate to patients | ● There were highly divergent views on the effectiveness of buprenorphine oral lyophilisate in terms of managing symptoms<br>● Whilst some patients described limited negative symptoms, others described a range of side effects, some that were akin to withdrawal symptoms. Some explicitly identified their symptoms as withdrawal symptoms using terms such as 'rattling' and 'clucking'<br>● For some the switch from Subutex took place with minimum impact on their physical symptoms, whilst others described several days of feeling unwell whilst they adjusted to the new medication. Some described a period of experimentation with dosage that took place over several weeks<br>● In general, the speed with which the medication dissolves was viewed by patients as a positive factor<br>● Size of dosage was linked to speed of dissolution<br>● Some associated the speed of dissolution with lack of efficacy in terms of the medication 'not holding' them, leading to withdrawal symptoms<br>● There were mixed opinions about the formulation of the tablet in terms of texture and taste; dependent on personal preference for the 'minty' taste |
| Impact on emotional wellbeing and relationships | ● Some patients reflected that they were feeling more emotional since the switch to buprenorphine oral lyophilisate but were unsure if this was due to the change in medication, coming off opiates in general, or changes in other psychiatric medication. Some attributed poorer emotional wellbeing with experiencing the severe side effects whilst on buprenorphine oral lyophilisate<br>● Most patients did not describe any changes in their relationships with friends, family and other prisoners as a result of the change in medication |
| Supervision process | ● Most patients did not think there were any major changes in the logistics of the supervision process apart from the speed, due to the fast dissolution of the medication<br>● Patients from both prisons described an initial period of confusion [of the administration process] whilst the staff came to terms with the correct administration period. This appeared to be linked with the administration of water to aid the dissolution process<br>● All patients described a process of constant surveillance during the administration process in order to ensure they were not concealing their medication |

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| The problem of diversion | ● Some patients provided details of how peers were able to divert the medication<br>● In general, patients in Leeds felt it was more difficult to divert buprenorphine oral lyophilisate in comparison to Subutex<br>● Some patients spoke about the ongoing pressures to divert their medication<br>● One patient stated the pressure to divert their medication was less with buprenorphine oral lyophilisate, and that this was due to the general awareness about the different formulation |
| Prison environment | ● Patients held different beliefs about the reasons why the prison had adopted buprenorphine oral lyophilisate to reduce diversion of Subutex and faster administration process<br>● In Leeds, the patients were of the opinion that it was difficult to get access to buprenorphine oral lyophilisate, and therefore only a handful of people were using it<br>● Some patients described feeling the stigma that comes with having an addiction problem, complaining that there was a lack of understanding and compassion among staff, both medical professionals and prison staff |
| Preference for opiate substitution treatment | ● Methadone was viewed as being particularly difficult to come off and therefore buprenorphine oral lyophilisate was viewed as being more congruent with treatment goals<br>● When asked about their preference for OST, a strong theme identified in the responses was the positive views about buprenorphine in general, rather than buprenorphine oral lyophilisate in particular<br>● There appeared to be differing views between the two prisons. Whilst in Pentonville there appeared to be a preference for Subutex, in Leeds patients overwhelmingly said they would recommend buprenorphine oral lyophilisate. Preference was associated with the effectiveness of either medication to manage symptoms |

OST, opioid substitution therapy.

**Supplementary table 2. Staff interviews.**

| Theme | Staff views |
|---|---|
| Clinical experience with OST medications | ● Staff saw between 13—17 patients a day with the principal medications consisting of methadone or buprenorphine |
| Staff views of OST medications | ● No side effects were identified by the staff interviewed, with the exception of one staff member who had noticed patients experiencing a rash<br>● Staff were of the general view there were less diversions with buprenorphine oral lyophilisate in comparison to other OST medications, but that some patients were still finding ways to conceal<br>● Concerns were expressed about the minimum level of dose available for buprenorphine oral lyophilisate (2mg) which is high in comparison to Subutex, and which makes detoxing a challenge |
| Preferences for OST medications | ● In general staff at Pentonville expressed a preference for buprenorphine oral lyophilisate because it dissolves quickly, stops craving, gives the full amount of the prescribed medication to the patient. Some staff in Leeds preferred methadone, namely because it is easier to manage, and they thought it led to less diversions<br>● Staff believed patients preferred buprenorphine because it is easier to detox from than methadone |

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| Supervision of buprenorphine oral lyophilisate | • Staff discussed how patients found buprenorphine oral lyophilisate more acceptable once they understood more about the medication, suggesting the importance of patient education and awareness raising to aid transition<br>• A few members of staff stated that it took some time to educate the patients in how buprenorphine oral lyophilisate will be administered<br>• Staff identified improvements in the administration of buprenorphine oral lyophilisate compared to other buprenorphine preparations: no need to crush the tablet, fast speed of tablet dissolution, less people to observe at any one time, and the ability to have several staff observe a patient at any one time<br>• Staff expressed continued concerns about the ability of patients to divert buprenorphine oral lyophilisate. Some staff expressed concern that they did not have sufficient understanding of how to carry out appropriate checks<br>• Some staff felt the logistics of accompanying patients between the pharmacy and the accommodation wing by the prison officers could be better coordinated<br>• Staff felt the speed of dissolution of the tablets differed between patients, and this was not necessarily linked to the dose |
| Behavioural impacts of changing medications | • There were mixed views as to whether prisoner intimidation had reduced as a result of the switch to buprenorphine oral lyophilisate.<br>• Some staff reported fewer challenges once patients understood the medication and the administration process<br>• Other staff described ongoing kick-back from patients when trying to challenge any suspected concealment or diversion |
| Impact on staff—patient relationship | • Several members of staff stated that there had been no impact on their relationship with the patients since the switch<br>• Other staff reported that their relationships had improved once they had been through the process of confronting the patient about suspected concealment, and had explained their reasons for doing so and their role as 'observer' in the supervision process |
| Impact on quality of life/work | • There were mixed opinions on the impact of the switch to buprenorphine oral lyophilisate on quality of life or work<br>• Whilst some staff noted no changes, others felt their job was easier because the administration process was shorter and there was less time spent dealing with concealment issues |
| Satisfaction with buprenorphine oral lyophilisate | • In general, staff expressed satisfaction with buprenorphine oral lyophilisate mainly due to the reasons expressed above<br>• One staff member suggested they had only experienced minimal impact of buprenorphine oral lyophilisate because only a few patients were being prescribed it |
| Change in illicit activities | • Some staff discussed the ongoing challenges of patients misusing (any) drugs and how some staff are not fully knowledgeable of how buprenorphine can be abused<br>• In general staff believed there was less diversion/concealment with buprenorphine oral lyophilisate, but that it is still taking place |
| Change in criminality among patients | • Some members of staff said there had been no changes in criminality and others stated that it is too early to tell |
| Impact on overall safety | • There was no mention of any observed impacts on the overall safety of the prisoners<br>• The majority of the staff did discuss an overall impact on the safety of their colleagues due to less time spent at the medication hatch, a decrease in |

| | |
|---|---|
| | aggressive and intimidating behaviour and fewer patients diverting/palming their medications |
| Staff regime and resource management | • Staff suggested that the introduction of Espranor® had positively impacted the daily routine and resource management. For example, one member of staff discussed the reduction in the medication queues, which ultimately saves money and time |

OST, opioid substitution therapy.