Microdosing: An Off-Label Titration Approach in Opioid Dependence

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Introduction

- Buprenorphine, a partial opioid agonist, is an alternative option to methadone for Opioid Substitution Therapy (OST) which may offer advantages and improved treatment outcomes for some people with opioid use disorder.
- Unfortunately, beginning treatment with buprenorphine can be challenging as the 'standard' approach requires a period of opioid agonist abstinence and experience of moderate withdrawal before initiation to prevent precipitation of a more abrupt withdrawal episode. This can cause anxiety and physical discomfort and presents a barrier to treatment.
- To provide alternative options for patients to transition safely to buprenorphine, a microdosing approach was developed as a component of a 'Toolbox' approach, which seeks to provide all necessary options for patients and prescribers to provide Realistic Medicine approaches to shared care, with informed patients able to access the full range of treatment options available, without needless barrier or restriction.

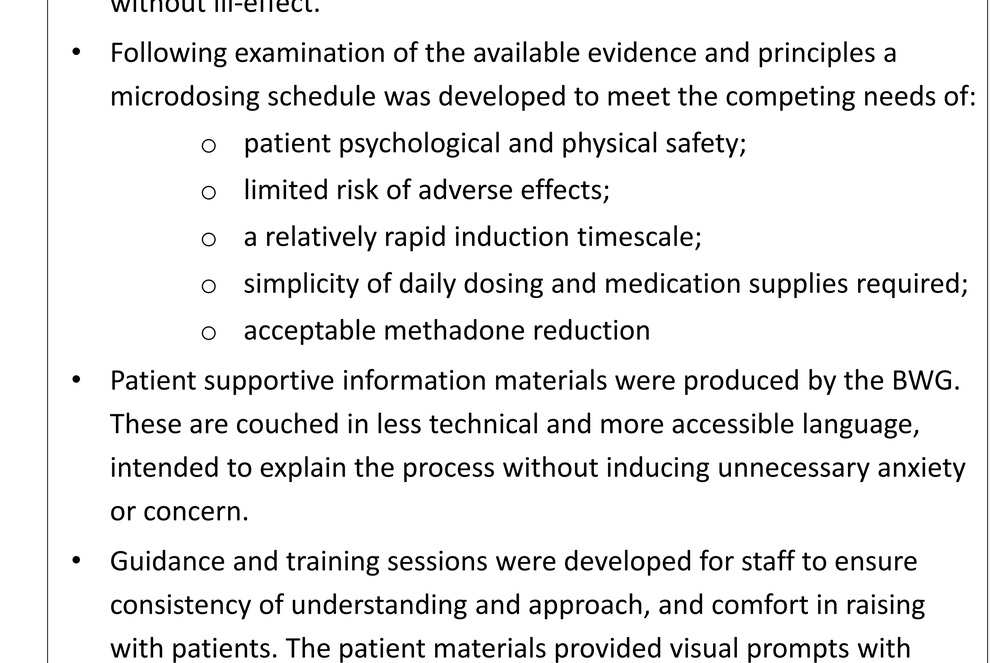
Aims

- Reduce barriers to patients' accessing buprenorphine-based OST.
- Provide a psychologically-supportive alternative route for patients to access buprenorphine-based OST
- Ensure prescribers have suitable options in their 'Toolbox'

Description of Work

- Buprenorphine microdosing, also known as the 'Bernese method', leverages the stronger receptor binding and lower intrinsic activity of buprenorphine to displace more active opioid agonists from the mu receptors in a dose-related manner (Hämmig, 2016). This competitive gradual displacement allows for a measured incremental cross-titration to achieve a therapeutic dose of buprenorphine without significant risk of a precipitated withdrawal. Once 16mg of daily buprenorphine is achieved approximately 95% of the mu opioid receptors are occupied by buprenorphine and unavailable to activation by other opioid receptors (Zubieta, 2000). Methadone remains in the system throughout but becomes clinically superfluous as it has little opportunity to affect opioid receptors and can then be rapidly reduced without ill-effect.
- Following examination of the available evidence and principles a microdosing schedule was developed to meet the competing needs of:
  - patient psychological and physical safety;
  - limited risk of adverse effects;
  - a relatively rapid induction timescale;
  - simplicity of daily dosing and medication supplies required;
  - acceptable methadone reduction
- Patient supportive information materials were produced by the BWG. These are couched in less technical and more accessible language, intended to explain the process without inducing unnecessary anxiety or concern.
- Guidance and training sessions were developed for staff to ensure consistency of understanding and approach, and comfort in raising with patients. The patient materials provided visual prompts with recommended terminology to support patient discussions.
- Explanatory letters for the community pharmacies were produced to inform partners of this novel way of working and to allow additional support of patients.
- These materials were iteratively redesigned and improved based on patient, staff and primary care partner feedback following test of change piloting of the processes by members of the BWG.

Patient Feedback

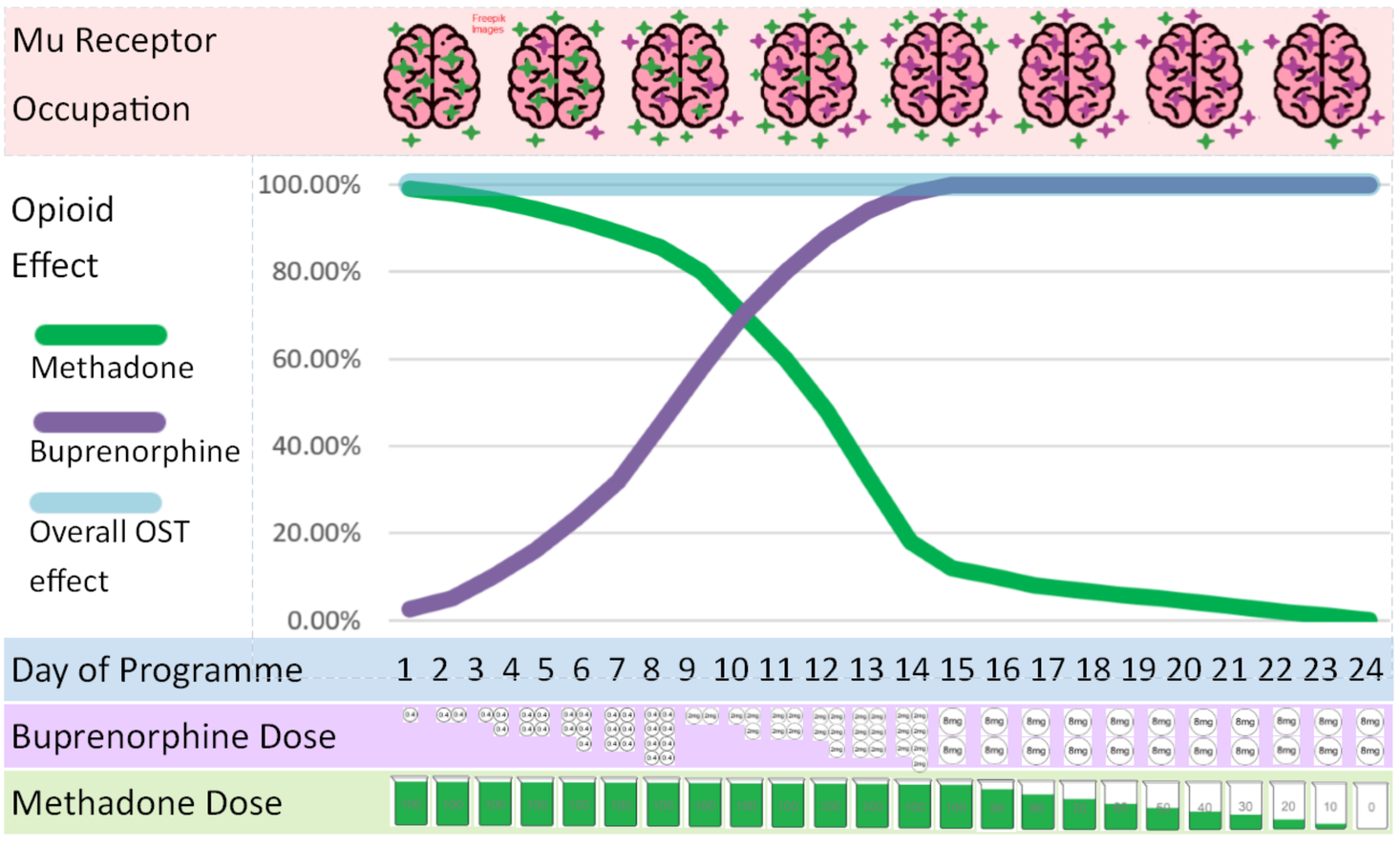


People Involved

The multiprofessional Buprenorphine Working Group (BWG) oversaw this work,. This group liaised with wider teams to inform, educate and provide an avenue for feedback.

Patients supported through a pilot microdosing process were asked to give feedback on their experience and the information materials provided.

Infographic of the Microdosing Process and Treatment Regimen

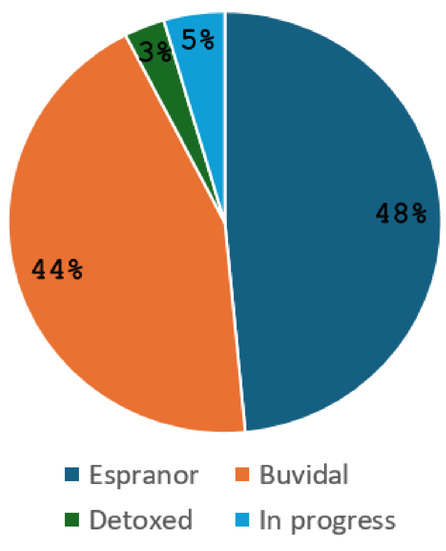


Outcomes

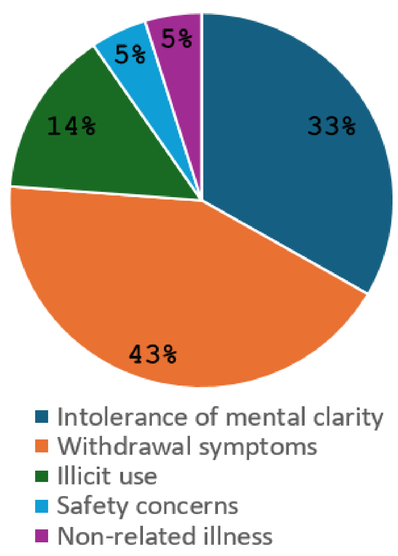
Since introducing microdosing in September 2023, **87** individual microdosing attempts have been initiated:

- **61** patients who have undergone microdosing are stable on a buprenorphine-based OST treatment - a **75.9% retention** on treatment following transfer.
- **21 patients (24.1%)** reverted to Methadone therapy.

Treatment Outcomes



Reasons Why Unsuccessful



Lessons Learned

- The principles of microdosing can be complex to explain simply and comprehensibly, and uncertainty led to concerns and hesitation. Supportive materials and training were necessary.
- Communication issues around community pharmacist awareness and concerns regarding the unusual prescribing.
- Logistical issues around supply validated the pilot approach taken.
- Patients may not be ready for the mental clarity afforded by buprenorphine – and that's okay!
- Concerns about safety and tolerability were raised.
  - Developed an audit process of SOWS scoring during the transition. Provisional finding that only 2/11 patients experienced more than mild symptoms throughout. Both had pre-existing issues affecting scoring (anxiety, hyperhidrosis)
- Need for evaluation of outcomes
  - A qualitative audit of microdosing experience is ongoing, alongside a wider assessment of 'soft' and quantitative outcomes' of OST treatment.

Conclusions

- **Patients are able to transition to buprenorphine therapy with minimal experience of withdrawal symptoms.**
- **More patients are able to access buprenorphine as their preferred OST with the availability of microdosing.**

References / Acknowledgements

Thank you to the members of the NHS Ayrshire and Arran Buprenorphine Working Group

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