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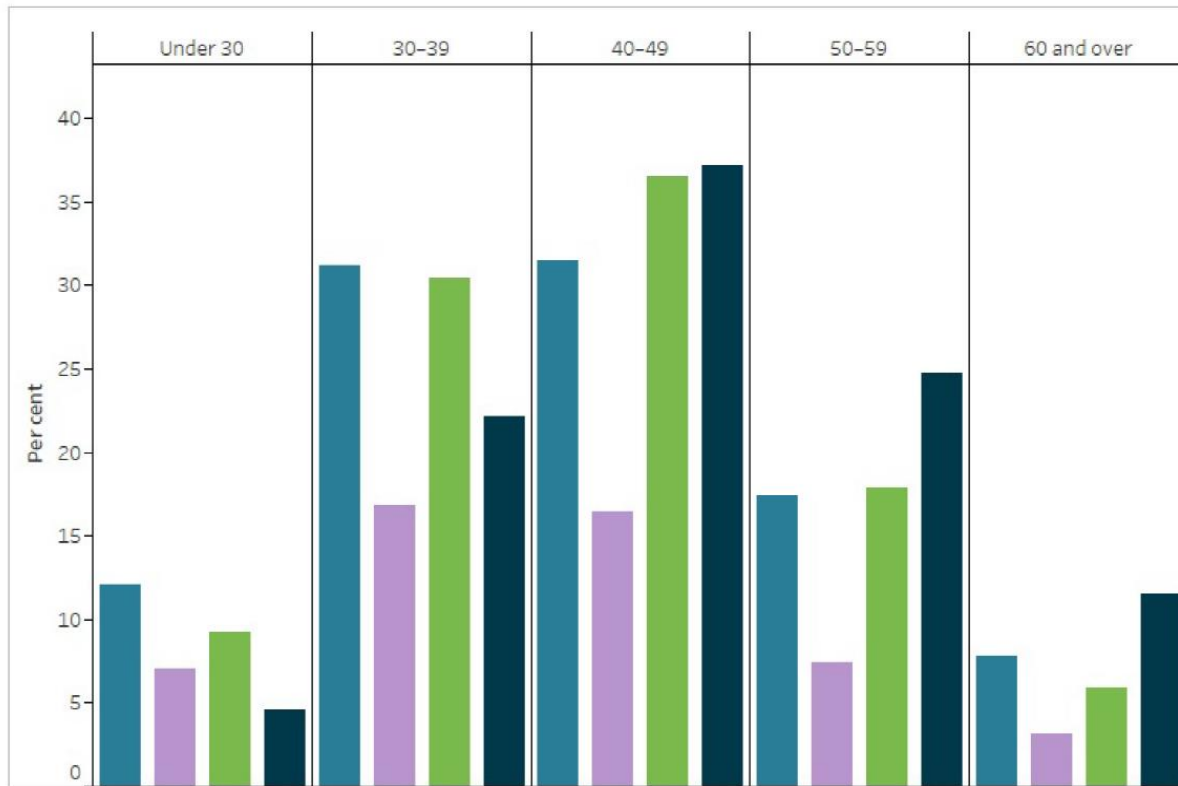


Methadone to LAIB - where are we at?

Victorian Opioid Management ECHO
Department of Addiction Medicine
St Vincent's Hospital Melbourne 2021

UNDER THE STEWARDSHIP OF MARY AIKENHEAD MINISTRIES

Starting point – mid-year 2020



Year
2020

Pharmacotherapy type

■ Buprenorphine

■ Buprenorphine LAI

■ Buprenorphine-naloxone

■ Methadone

Dilemma



Older age group on methadone

- Often long durations of methadone
- Substantial variation across age groups of buprenorphine vs methadone
- Cohort is aging

Pharmacology

- Major risk is precipitated withdrawal
- Methadone to buprenorphine most difficult transfer
- Bridging?
- Transfer to short acting opioids?

Right reasons?

What advantages from transfer?

Set clear expectations – very individualised decision

Is it ok to go back?

Careful that we are not potentially destabilising an otherwise well patient

Risks in transfer

Can this problem be solved in any other way? (take away methadone doses, stopping the benzodiazepines and sedating antipsychotics, enhanced psychosocial care etc...)

Baseline Protocol

TABLE 1. Overview of Clinical Guidelines for Transferring From Methadone to Buprenorphine

Assessment, treatment planning, and patient education—examine patient expectancies, reasons for transfer, and discuss transfer procedures. Identify, and where possible stabilize, any risks for patient safety during the transfer, including unstable substance use, physical, mental health, or social conditions

Unless urgent transfer required (eg, severe side effects to methadone), gradually reduce methadone dose until patient starts to experience mild to moderate opioid withdrawal between doses

Consider treatment setting: inpatient settings recommended for patients transferring from high methadone doses or significant health comorbidities or unstable social conditions

Cease methadone and monitor the patient regularly (at least daily) for evidence of opioid withdrawal symptoms. Initiate buprenorphine treatment when patient experiencing moderate opioid withdrawal severity (Clinical Opioid Withdrawal Scale [COWS] >12), at least 24 h after last methadone dose

Initiate low-dose buprenorphine treatment (2 mg), and monitor hourly for evidence of precipitated withdrawal, preferably using a withdrawal scale (eg, COWS). Administer further 6 mg after 1 h. Further doses (4 or 8 mg at a time) are symptom-triggered, and continue regular monitoring and dosing until patient comfortable

On subsequent days, buprenorphine dose = previous days dose + additional dose based upon withdrawal severity (symptom triggered)

Transferring Patients From Methadone to Buprenorphine: The Feasibility and Evaluation of Practice Guidelines

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(J Addict Med 2018;12: 234–240)

n=33, 4 Australian centres
 low dose < 30mg
 medium 30-50 mg
 high Dose > 50mg

TABLE 2. Summary Data Regarding Transfers by Dose Categories

	Low-dose Transfer (n = 9)	Medium-dose Transfer (n = 9)	High-dose Transfer (n = 15)	Significance
Setting for transfer				
Inpatient	2 (22%)	4 (44%)	14 (93%)	<i>P</i> < 0.05
Outpatient	7 (78%)	5 (56%)	1 (7%)	
Adherence to guidelines				
Yes	7 (78%)	6 (67%)	10 (67%)	NS
No	2 (22%)	3 (33%)	5 (33%)	
Did precipitated withdrawal occur?				
Yes	0	0	3 (20%)	NS
No	9 (100%)	9 (100%)	12 (80%)	
In BNX treatment 7 d after transfer				
Yes	8 (89%)	8 (89%)	10 (67%)	NS
No	1 (11%)	1 (11%)	5 (33%)	

BNX, buprenorphine-naloxone; NS, not significant.

Low and medium doses (up to 50mg)

- anticipate success
- little need to do anything more than above protocol

➤ 50mg

- Still get at least 2/3rds success with above

Higher baseline methadone required higher dose buprenorphine within first 2 days

And



Unpublished presented at APSAD (Australian)

- 8 patients transferred directly from oral methadone to LAIB
- both inpatient and outpatient
- Generally reduced to methadone < 40mg
- Initiated at Buvidal Weekly 16mg – without supplemental sublingual buprenorphine

New program through Camarus

- enables prescriber to access two 8mg and 16mg Buvidal weekly prior to first prescription (either at clinic or through chosen pharmacy to hold)
- transfer from methadone to LAIB not included (within label but not PBS)

START Weekly
+ STABILISE WITH Buvidal®
BUPRENORPHINE

PRODUCT
FAMILIARISATION
PROGRAM (PFP)

Switching from long-acting opioids (e.g. methadone)

When switching patients from methadone, the dose of methadone should be reduced to a maximum of 30 mg/day before starting treatment with Buvidal®. Buvidal® should not be administered until at least 24 hours after the patient last received a methadone dose. Buvidal® may trigger withdrawal symptoms in methadone-dependent patients.¹ Please read the full Prescribing Information for Buvidal® Weekly and Buvidal® Monthly before initiating.

Micro-induction and Bridging

- underlying principle of methods of transfer

The Bernese method

The Bernese method has been the basis of many unique methods of starting buprenorphine. The authors of this method determined the following²⁴:

- (1) Repetitive administration of very small buprenorphine doses with sufficient dosing intervals (e.g., 12 hours) should not precipitate opioid withdrawal.
- (2) Because of the long receptor binding time due to higher affinity, buprenorphine will accumulate at the receptor.
- (3) Over time, a greater percentage of the full μ -agonist will be replaced by buprenorphine at the opioid receptor as the dominant opioid.

LIMITATIONS

Outside of the standard treatment method outlined in the *Reasons for transitioning from methadone to buprenorphine* section, there is limited evidence to substantiate any of the novel methods described. There are no efficacy trials done, and there is limited data comparing one method to the other. Clinical trials are undeniably required to appropriately and firmly establish these protocols in our armamentarium. Future trials should examine the starting dose of methadone before transfer (low <50 mg, medium >50–100 mg, or high dose >100 mg), withdrawal risk, transfer completion rates, the efficacy of the speed of up-titration of buprenorphine, and retention rates.

A Review of Novel Methods To Support The Transition
From Methadone and Other Full Agonist Opioids To
Buprenorphine/Naloxone Sublingual In Both
Community and Acute Care Settings

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Options

TABLE 1 | Examples of various buprenorphine microdosing schedules.

	Day	1	2	3	4	5	6	7	8	9	10	11
1. Bernese method (20)	Dose (mg)	0.2	0.2	0.8 + 2	2 + 2.5	2.5 bd	2.5 + 4	4 bd	4 bd	8 + 4	Titrate PRN	
2. Terasaki et al. (2019) (20)	Dose (mg)	0.5	0.5 bd	1 bd	4 bd	8	8 + 4	12		Titrate PRN		
3. VCH (22)	Dose (mg)	0.25	0.25 bd	0.5 bd	1 bd	2 bd	4 bd	12		Titrate PRN		
4. Lu & Cho (2018) (22)	Dose (mg)	0.5 bd	1 bd	2 bd	3 bd	4 bd	12	16		Titrate PRN		
5. Used in this study	Dose (mg)	0.4	0.4	0.8	1.2	1.6	1.6	2	4	6	8–12	16

VCH, Vancouver Coastal Health bd twice a day. PRN as required.

In microdosing method 1 and 5, the patient tapers down on their full agonist on day 7 to a full stop by day 11. In methods 2,3 & 4, cessation of the full agonist should happen on day 7.

Using Microdosing to Induct Patients Into a Long-Acting Injectable Buprenorphine Depot Medication in Low Threshold Community Settings: A Case Study

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TABLE 3 | Summary of patient characteristics and case histories.

Case Number	Gender	Age (years)	Primary opioid/s daily use	Reason for patient selection	Microdosing regime start to first depot (Days)	Depot buprenorphine dose and frequency
1	M	36	Methadone 75 mg Prescribed	Treatment failure with sublingual buprenorphine, methadone and naltrexone implant	14	96 mg monthly
2	M	45	Heroin 0.5–1 g inhaled	Treatment failure on both sublingual buprenorphine and methadone. Required to shield due to severe COPD.	19	96 mg monthly
3	F	51	Heroin 0.5–1 g snorted	Treatment failure on both sublingual buprenorphine and methadone. Frequent disengagement from services due to employment. Required to shield due to severe COPD.	8	96 mg monthly
4	M	42	Heroin IV 1 g and methadone 80 mg prescribed	Treatment failure with methadone and with residential rehabilitation. Multiple deliberate and accidental overdoses. Due to polysubstance use and pandemic restrictions, struggled with regular pharmacy attendance. HIV positive with ongoing IDU.	13	128 mg monthly
5	M	46	Heroin IV 1 g, and methadone 40 mg prescribed	Treatment failure with methadone. Frequent episodes of acute renal colic resulting in a need for A/E admission and analgesia, disrupting dose collection at pharmacy. Difficulty in ceasing IDU. HIV positive	13	128 mg monthly

M- Male F- Female. COPD- Chronic Obstructive Pulmonary disease. HIV- Human Immunodeficiency Virus. mg-miligram. g-grams. IDU- intravenous drug use.

trials. There have however been case reports and substantial practical experience with this method in Canada, Germany and locally in the South East and the West of Scotland (Cassells et al., 2020). The result is a broad range of regimens with no consensus on optimum dosing.

Microdosing – useful in a minority?

Methods possible but complicated, little consensus, case reports only, follow the principles

Do we already have a process for the vast majority of transfers?

Using heroin is not a good option but it may be reasonable to ask the question – can we as clinicians live with that outcome when we are attempting these transfers
- would they remain engaged enough to then commence LAIB direct from heroin

Host of regulatory issues

