# **A bridge too small: A case series of microdosing transfers from oral methadone to depot buprenorphine** Paper 8

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As dependency treatments Opioid Agonist Therapy (OAT) provide evidence-based harm minimisation utilising methadone or sublingual buprenorphine (SLB). Despite our investment in supervision, diversion and misuse is common. The advent of depot buprenorphine (DB) side-steps concerns about injecting, overdosing or diversion. DB is subsidised by the Commonwealth government, while other formulations of OAT are not. During the COVID pandemic, use of DB facilitates a reduction in close contact between staff and consumers.

The transition from sublingual to DB is straight-forward, unlike that from methadone or other opioid agonists. Due to its stronger receptor-binding affinity, the partial agonist buprenorphine displaces other pre-existing opioids through competitive inhibition risking a precipitated withdrawal. Along with the classical physical opioid withdrawal, this may cause an overwhelming emotional hypersensitivity and pain (1). To reduce the risk of precipitated withdrawal, guidelines advise to reduce the methadone dose to levels as low as 30mg before ceasing opioids for 48 hours (2, 3) and then commencing 2-4mg SLB. Because methadone metabolites may last weeks (4), the standard approach and its staged withdrawal still risks a further precipitated one.

An innovative “Bernese” method has been described in Switzerland and North America (3). Microdoses of buprenorphine (sublingual, transdermal or IV (5)) are steadily increased while reducing or maintaining the methadone dose. The methadone is

withdrawn once the buprenorphine levels are sufficient to have displaced it. SLB alone is continued for 4 to 5 methadone half-lives to clear its metabolites, before commencing DB (4). Two literature reviews have described 26 different approaches across 18- 20 low quality case studies/series and one feasibility study (n= 57 or 63 patients) (2, 6, 7).

I am a GP and part-time addiction specialist in rural NSW and the conjunction of the COVID pandemic and arrival of DB motivated me to explore these transition methods. My narrative will sketch the 10 varied approaches I trialled in 9 patients, with their disparate outcomes as well as my attempts at patient recruitment and education. This was done in a time poor outpatient context with limited supervision or support options and involved a group selected by neither dose nor stability. A patient information brocheure was developed with feedback from patients and Anne Fredrickson, social worker. To my knowledge, this is the first patient information brocheure on microdose transfers. While the microdose transfer system had been used in South Australia, NSW Health informed me that state legislation prohibited prescribing both opioids simultaneously. However, my application for patient 6 was their first application received and approved.

**Patient 1:** JA 48yo Caucasian male post oesophagectomy for oesophageal cancer 2008. I consulted him in 2018, when his analgesia regime was 75-150mcg fentanyl patches every 2-3 days as well as methadone 35mls (175mg). By January 8, 2020, his prescriber had relinquished his methadone authority and declined further care, referring him to me again. I assumed his opioid care January 20 when he informed me that he had run out of fentanyl. (Later he confessed that he was actually on Day 2 of his last patch!) He was in frank withdrawal with evidence of IM injecting. I commenced 1mg SLB with a 1mg takeaway at a

private pharmacy. The next day he took 4mg with a 4mg takeaway plus melatonin. He reported no withdrawal. He had 8mg + 8mg the next day and reported his first decent sleep. On March 2, we switched from 32mg SLB to DB (buvidal®). He found buvidal injections painful and reported inadequate analgesia on 128mg monthly. We switched to DB sublocade® 300mg (which he prefers to 100mg). His physical and family health is improved with this regime and his cachexia is less.

**Patient 2:** CC 37yo Caucasian male August 8, 2020. During the year we had planned to reduce his methadone from 100mg to 60mg at his private pharmacy, but he kept reducing to 40mg. We had one day methadone free, then SLB 0.2mg (temgesic®) one twice a day for one day, two twice a day the next and 2mg suboxone bd the following day. Two weeks later, I reviewed him. He said while the withdrawal was "hairy", that taking the temgesic had helped. Now his thinking was far clearer on SLB 16mg. At last review January 2021, he is surfing daily, planning to get married and enjoying visiting the pharmacy and so has decided not to switch to DB.

**Patient 3**: JC 31yo aboriginal male released from jail July 24 2020. He had been on 60mg methadone and found each dose lasted 2 days. We consulted August 18, when he had missed five doses, attended two and agreed to not dose that day. The next day he had SLB subutex® 0.4mg with 0.8mg the next and suboxone 2mg on Day 3. On Day 6, he was re-incarcerated. He has since been released and is doing well on 128mg buvidal monthly.

**Patient 4:** PB 33yo Aboriginal male a regular ICE user with past traumatic brain injuries. On September 8, 2020, he was keen to switch from 35mg methadone to suboxone, but not DB. Day 1: no methadone and transdermal buprenorphine (norspan ®) 5mcg

patch, Day 2 norspan 5mcg added, Day three suboxone 2mg begun with a rapid increase to 32mg where he remains. The transition was uneventful but concerns about ICE use and diversion of his suboxone dose remain.

**Patient 5**: JC 28yo Aboriginal male with past bipolar, polydrug use and multiple incarcerations. Since July he had reduced methadone from 110mg to 60mg. On September 9 he was provided with 60mg methadone, one 0.2mg temgesic stat with one to take home. He next presented Sept 12. He refused to cooperate with a COWS withdrawal assessment and reported using $50 of Heroin the previous night for withdrawals. He ceased attending and is currently incarcerated.

**Patient 6 (& 10)**: MB 51yo Caucasian male. Past: OCD, abuse of diazepam, cannabis, ICE and heroin (&/or "home-baked" opioids), recent fractured skull from an assault. On methadone 57.5mg at a private pharmacy. Over 4 days, from September 14, his methadone was reduced to 15mg and temgesics increased to 4 bd (1.6mg). Temgesics are not on PBS and their cost was a barrier. On Saturday 19th, the pharmacist wanted to close but rang as MB was demanding to stay on 15mg methadone and not start "the blocker" (suboxone). After speaking to them both, we arranged for MB to stay on these same doses till Monday 21st when he would cease methadone and commence an escalating dose of suboxone. He did not attend his appointment on 22nd. On Sept 25, the pharmacist told me he was OK though "cranky" on suboxone 2mg only and wished to remain on this dose. I sanctioned an increasing optional regime. MB next consulted me November 17. He said he had been stuck three weeks on suboxone 2mg and so used heroin every day. He had since increased to suboxone 24mg and was feeling clearer in the head. He said the switch was overall worthwhile and that he had

recommended this transition to others. (Others told me he deterred them!) He switched to weekly buvidal and then 128mg monthly.

**Patients 7 & 8**: had different methadone reduction regimes but identical norspan regimes scheduled from October 14, 2020. Days 1 and 3, 10mcg; Days 5 & 7, 20mcg.

**Patient 7**: ES 25yo Aboriginal male on 90mg methadone which was insufficient. His methadone was reduced by 1/3 on Days 3, 5 & 7. He managed the withdrawal which made his 3° burn scars "tingle" by increasing his cannabis. He is "stoked" to be doing well on 128mg buvidal.

**Patient 8**: MNB 39yo Aboriginal male. Passive aggressive, multiple incarcerations on methadone 80mg plus twice a week injecting heroin into jugular vein. At a phone consult, we decided to switch via a microdose bridge and to reduce his dose 20mg every second day from Day 1. On 16th (Day 3) he refused to reduce his dose from 60mg to 40mg as could not sleep. No signs of withdrawal, reportedly, so norspan 10mcg applied. He failed attend Day 5 (18th) but he had a 20mg patch applied on 19th and 20th October. On 20th, he removed the new 20mcg patch after it was applied due to pruritis. He was pale and described withdrawals worsening after the previous day's patch. He was given 2mg suboxone. That afternoon, he re-presented in withdrawal. He was given 4mg Suboxone. He returned one hour later in severe withdrawal (COWS 24). He was given 20mg methadone and returned an hour later. His withdrawal had reduced though he reported being uncomfortable. He was given another 20mg methadone. He then advised that he had used heroin and ICE after that morning's suboxone. On Day 8 (21st) he reported aches, restlessness and insomnia. His COWS showed mild withdrawal. He was provided 40mg methadone and

suboxone 2mg with these doses repeated on Day 9 (22nd). He returned that afternoon and reported less sweating with a COWS withdrawal score of 20. He was given an extra 20mg methadone. On Day 10 (23rd) he refused suboxone and was returned to 60mg methadone.

In late December 2020, he missed five days dosing due to a family funeral in Sydney. During this time, he used alprazolam and injected heroin requiring an admission for an overdose. He recommenced 60mg methadone and remains on this dose.

**Patient 9**: DP 33yo Caucasian male using IV heroin. Past ADHD, anxiety, THC use presenting with possible mania. He agreed to start OAT after he finished his stash of heroin. Day 1 (December 8 2020) temgesic 0.2mg stat with three takeaways. Seen Day 2 with a COWS 19. He had taken all his doses at once, which had reduced the withdrawal. We provided suboxone 2mg and 2mg takeaway dose. Over 4 days, he moved to 32mg and after 2 weeks to buvidal 128mg monthly.

**Patient 10 (aka patient 6)**: MB again, had been doing so well on buvidal 128mg monthly, that he decided to cease attending. On February 2, 2021, he re-presented having relapsed to heroin use. He denied heroin since the day before and he was in withdrawal. The public dosing facility provided him 0.2mg temgesic stat and one takeaway, 0.4mg + 0.4mg the next day and 2mg suboxone the third. He recommenced buvidal Day 4 with no reports of withdrawal from the dosing staff. He informed staff that in September the pharmacist had encouraged him to swallow his temgesics.

There would have been another 30 patients on methadone with whom I discussed a transfer. We completed the paperwork for one, but he postponed it due to the cost of the temgesic. One declined as their friend (patient 6/10) scared her off. Several had

needle phobias. Some were concerned when I explained this was experimental in Australia, rather than mainstream. Most were concerned about being de-stabilised or facing a withdrawal. An additional barrier was our prolonged of script durations with few face-to-face consultations due to the COVID pandemic.

## Conclusion

In this small prospective case series:

- Pre-transfer Methadone doses ranged from 35mg to 90mg, with two on heroin or other street opioids and one on transdermal (plus IM) fentanyl.
- First dose of SLB ranged from 0.2mg to 2mg.
- Duration till suboxone commenced:  Day one (1 patient); two (1); three (4); seven (1), eight (1).
- Three used heroin to cope with the transition.
- Outcomes: 7 transitioned to DB, 2 to suboxone, one returned to methadone and one ceased dosing.
- Retention: 8 of the 9 discrete patients remain on OAT.

Main lessons learned:

- Do not reduce methadone at all until a significant dose of SLB is reached (12-16mg).
- Temgesics and symptomatic treatments may be unaffordable and a twice daily dosing regime risks non-compliance.
- Documenting and managing withdrawals requires closer management than provided here. Contrarily, due to COVID, Dr Ken Lee in Canada is utilising a complete one-week, self-dosing package (private communication).

- There is a need to prepare out-patient protocols to cover missed doses and to equip private pharmacists.

Finally, the liberal use of opioid analgesics in chronic pain has seen commensurate increases in rates of refractory pain, depression, addictions, overdose and deaths. Given that buprenorphine has anti-hyperalgesic properties and is safer in overdose, the microdosing method may allow a paradigm shift in chronic opioid provision for pain (8).

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