Do dependent codeine users need lower doses of buprenorphine maintenance?

Mark Daglish[1,2], Sarah Reilly[1], Jeremy Hayllar[1]
[1]Metro North Hospital and Health Service – Alcohol and Drug Service, Brisbane, Australia,
[2]The University of Queensland, Brisbane, Australia

Metro North Hospital and Health Service *Putting people first*

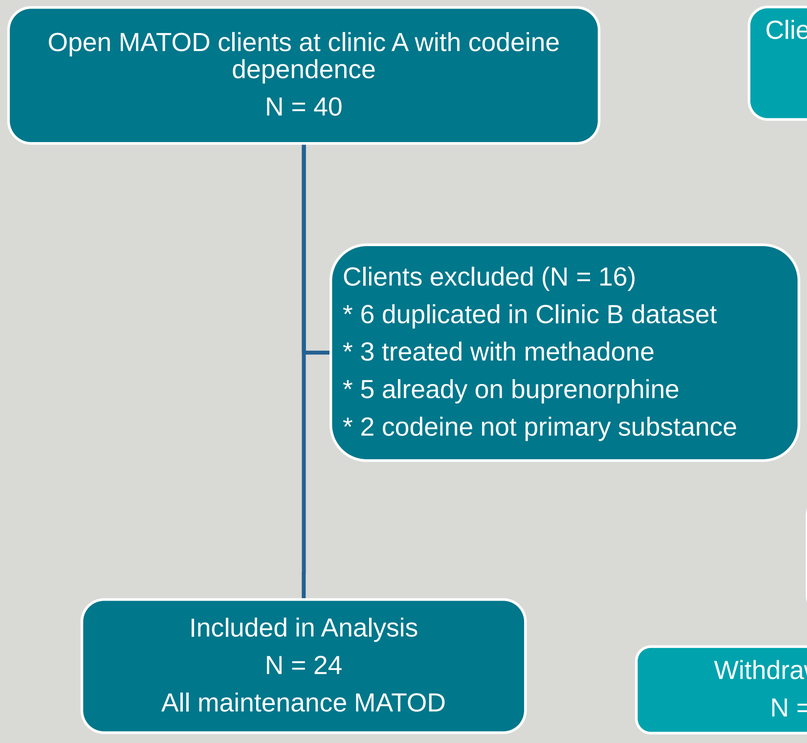
Background & Aims

In Australia on 1st Feb 2018 combination analgesics containing codeine (CACC) ceased to be available from pharmacists, becoming prescription-only, as a result of harms from their over use[1,2]. Existing Medication Assisted Treatment for Opioid Dependence (MATOD) guidelines for the management of illicit opioid dependence with buprenorphine* suggest most clients require a maintenance dose of 8 to 24mg[3]. Queensland public services target 40% MATOD retention rate at 12 months[3]. This study reviewed the appropriateness of these guidelines in the management of codeine dependent clients, focusing on demographics and buprenorphine requirement.

Methods:

This study presents a retrospective clinical audit of clients presenting with primary codeine dependence to two city MATOD clinics. As a pilot, case managers at clinic A identified active clients receiving MATOD with a history of codeine dependence, regardless of presentation date. To obtain a more representative sample at clinic B, a database search identified all clients presenting with codeine dependence between 1/1/16 and 30/6/18 for either MATOD or withdrawal management. Paper based charts were reviewed and demographics & treatment data were extracted by two clinicians, independently. This study was approved as a quality improvement project by the local human research ethics committee.

Flow of participants - Clinic A



Flow of participants - Clinic B

Table 1	Clinic B withdrawal	Clinic B maintenance MATOD	Clinic A maintenance MATOD
	N (%) or Mean ± SD	N (%) or Mean ± SD	N (%) or Mean ± SD
Number of participants	22	60	24
Age (years)	37 ± 8.9	37 ± 11	37 ± 8.8
Male : Female : Transgender	13(59%) : 9(41%) : -	31(52%) : 27(45%) : 2(3%)	7(29%) : 17(71%) : -
Employed	10 (45%)	24 (40%)	12 (50%)
Unemployed	4 (18%)	15 (25%)	6 (25%)
Pension	5 (23%)	19 (32%)	6 (25%)
Student	3 (14%)	2 (3%)	-
Pain previous	4 (18%)	17 (28%)	2 (8%)
Pain current	5 (23%)	24 (40%)	15 (63%)
NSAID/Paracetamol complications	4 (18%)	12 (20%)	7 (29%)
Mental health history	18 (82%)	54 (90%)	22 (92%)
Current Anti-depressant	13 (59%)	38 (63%)	20 (83%)
Previous MATOD hx	9 (41%)	19 (32%)	2 (8%)
Current other opioid	1 (5%)	14 (23%)	2 (8%)
Previous other opioid	4 (18%)	11 (18%)	6 (25%)
Tobacco Use Disorder	12 (55%)	36 (60%)	17 (71%)
Alcohol Use Disorder	7 (32%)	14 (23%)	7 (29%)
Amphetamine Use Disorder	3 (14%)	6 (10%)	3 (13%)
Cannabis Use Disorder	9 (41%)	12 (20%)	9 (38%)
Hx of IV drug use	1 (5%)	7 (12%)	3 (13%)
Childhood trauma	4 (18%)	23 (38%)	11 (46%)

Figure 1: Relationship between codeine & buprenorphine doses

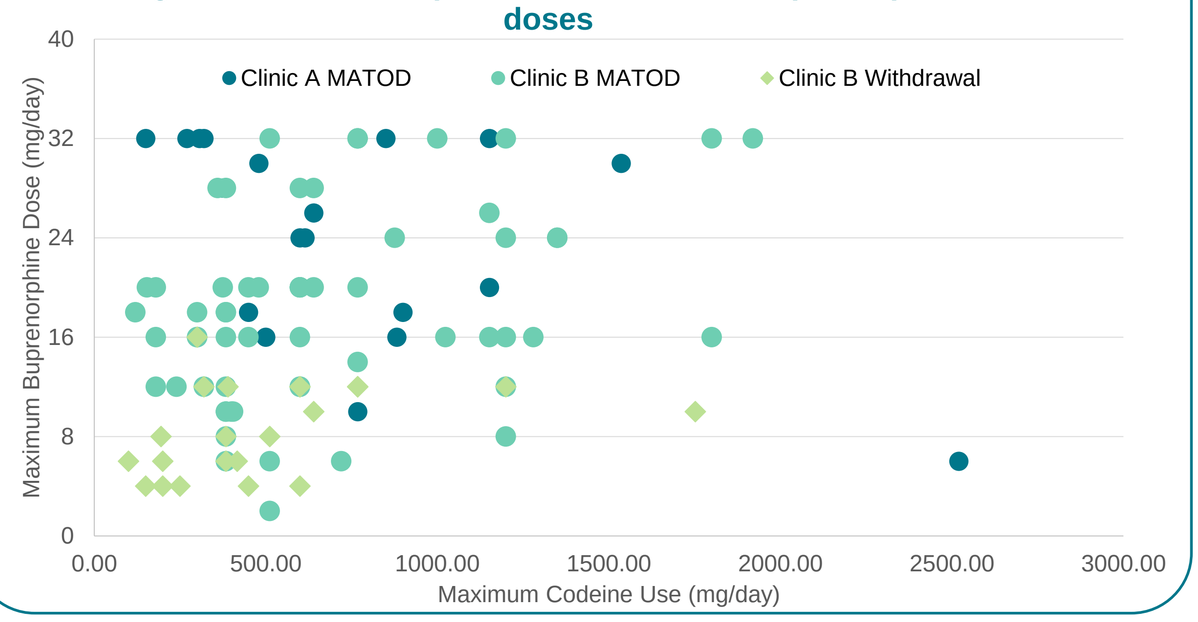


Table 2	Clinic B withdrawal	Clinic B maintenance MATOD	Clinic A maintenance MATOD
	N (%) or Mean ± SD	N (%) or Mean ± SD	N (%) or Mean ± SD
Codeine use (mg/day)	508 ± 377	679 ± 435	726 ± 516
Codeine use duration (years)	2.4 ± 3.1	4.3 ± 3.6	5.8 ± 6.5
MATOD duration	7.0 ± 3.7 (days)	1.0 ± 0.7 (years)	5.2 ± 3.3 (years)
Stabilised^ buprenorphine (mg)	-	15 ± 7.5	16 ± 7.3
Maximum buprenorphine (mg)	8.6 ± 3.6	18 ± 7.8	24 ± 7.7
Current buprenorphine (mg)	-	17 ± 9.2	19 ± 8.6
MATOD ≥ 1 year duration	-	28 (47%)	22 (92%)

Results

There were 106 treatment episodes where 102 codeine dependent clients were commenced on buprenorphine. The mean codeine doses, maximum and current buprenorphine doses at both clinics were recorded (Table 2). There was no significant relationship between the stated dose of codeine at presentation and the maximum dose of buprenorphine required during either withdrawal or maintenance MATOD (Figure 1). Clients seeking withdrawal management typically had a shorter duration of codeine use and a lower mean dose of codeine than clients requiring maintenance treatment.

At 12 months, 49% of clients in clinic B were still engaged in MATOD, exceeding the 40% retention goal set by the 2018 Queensland MATOD clinical guidelines. Contrary to expectation, the frequency of new clients presenting with codeine dependence decreased after February 1st 2018, with perhaps a spike at the end of 2017 (Figure 2).

Figure 2: Clinic B New opioid registrations per quarter

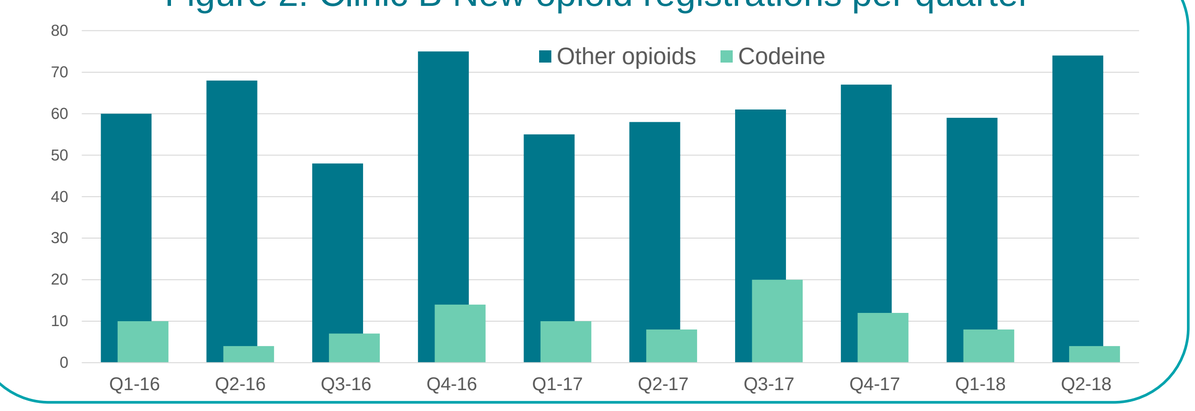
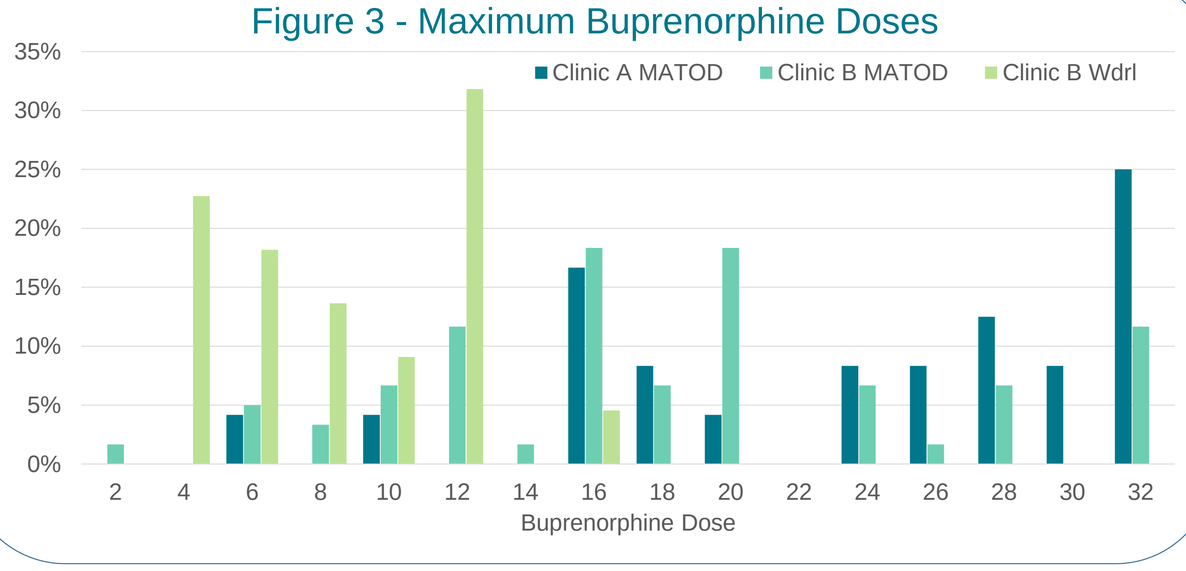


Figure 3 - Maximum Buprenorphine Doses



Discussions and Conclusions:

This study highlights the complexity found in this group of codeine dependent clients; with high rates of childhood trauma, depression, chronic pain and polysubstance use. Buprenorphine requirements were similar to those expected of illicit opioid users (Figure 3). Thus, the characterisation of codeine as a "weak" opioid, implying the need for lower doses of opioid substitution medication, is inaccurate. Dose estimation is difficult, with codeine dose at presentation a poor indicator of buprenorphine requirement. In part this may reflect the pharmacokinetics of codeine; with rates of codeine conversion to morphine dependent on CYP2D6 activity. Surprisingly, presentations related to codeine significantly decreased after CACC rescheduling to prescription medication only.

Implications for Practice:

Service guidelines should be adapted to accommodate the wide MATOD dose ranges that may be required by clients presenting with primary codeine dependence. Doses of buprenorphine required in those presenting with codeine dependence appear similar to those presenting with illicit opioid dependence[4,5]. Retention remains an issue and Alcohol and Drug services must strive to address the needs of the broad spectrum of clients with opioid dependence

Notes: *Buprenorphine is used throughout for brevity but refers to both buprenorphine-mono and buprenorphine/naloxone combination products. ^Stabilised buprenorphine is the dose when transitioned from daily dosing in clinic to community pharmacy dosing.

Acknowledgements: The authors would like to thank Deb Casperson, Jason Dalla Lana and David Mines for their assistance in conducting the audit.

REFERENCES:

1. Cock V, Edmonds C, Cock C. Complications related to chronic supratherapeutic use of codeine containing compound analgesics in a cohort of clients presenting for codeine withdrawal. Drug and Alcohol review. 2018;37(6):731-
2. Frei MY, Nielsen S, Dobbin MD, Tobin CL. Serious morbidity associated with misuse of over-the-counter codeine-ibuprofen analgesics: a series of 27 cases. The Medical journal of Australia. 2010;193(5):294-6.
3. State of Queensland (Queensland Health). Queensland Medication-Assisted Treatment of Opioid Dependence: Clinical Guidelines 2018. 2018
4. Nielsen S, Bruno R, Degenhardt L, Demirkol A, Lintzeris N. Opioid agonist doses for oxycodone and morphine dependence: Findings from a retrospective case series. Drug and Alcohol review. 2017;36(3):311-6.
5. Nielsen S, Murnion B, Dunlop A, Degenhardt L, Demirkol A, Muhleisen P, et al. Comparing treatment-seeking codeine users and strong opioid users: Findings from a novel case series. Drug and Alcohol review. 2015;34(3):304-11.