



# The UNLOC-T Trial: Implementing Depot Buprenorphine in NSW Correctional Facilities

Dr Adrian Dunlop MBBS PhD GdipEpiBiostat FACHAM FISAM

Director & Senior Staff Specialist, Drug & Alcohol Clinical Services, Hunter New England Local Health District  
Conjoint Professor | School of Medicine and Public Health, Faculty of Health, University of Newcastle

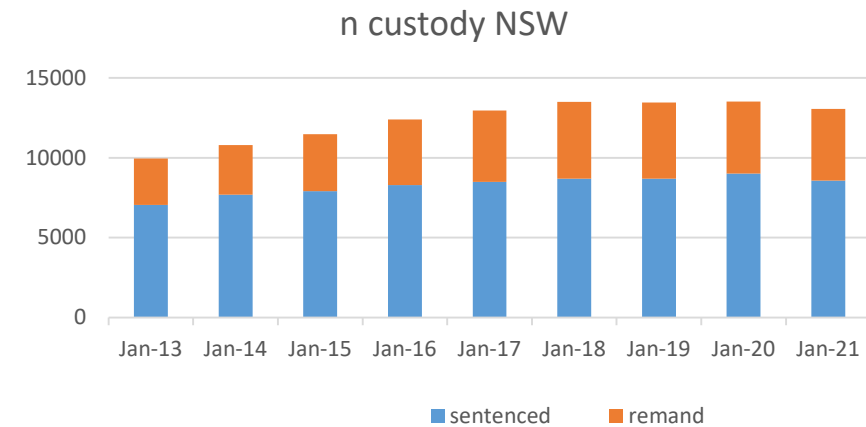
# Disclosures

- A.D. reports grants from Braeburn/Camurus AB, to conduct clinical studies with buprenorphine formulations and travel support to Hunter New England Local Health District, which employs A.D
- A.D is an investigator on an Indivior-funded study of a long acting buprenorphine formulation (Sublocade)
- A.D has served as an honorary on an advisory boards for Mundipharma & Seqirus

# Summary of literature – OAT in custody/on release

Finding	NHMRC level of evidence	Author
OAT associated with reduced drug use in prison	Level I	Moore 2019, Hedrich 2011, Stallwitz 2006, Malta 2019 ( <u>not</u> Perry 2015)
OAT in prison associated with reduced deaths in prison	Level III-2	Larney 2012
OAT in prison is cost-effective	Level III-3	Gisev 2015
People who use opioids have an increased mortality post release from custody	Level I	Merrall 2010
OAT associated with reduced mortality post release	Level III-2	Marsden 2017
OAT initiated in prison associated with increased engagement post release	Level I	Moore 2019, Heidrich 2011
OAT initiated on release not associated with engagement in treatment or reduced mortality	Level III-2	Pierce 2018
OAT in prison associated with reduced crime post release	Level I	Perry 2015

# Background



- Expansion in incarceration in NSW, Australia – 1/3 ↑
  - Over-crowding, movement between prisons ++
- Up to 2020: opioid agonist treatment (OAT) available
  - Continuous OAT: methadone >> SL BPN/NX
  - If not in treatment on entry – usually not offered treatment
  - Demand exceeds supply: under-treatment
- Significant problem with injecting use of (illicit) SL BPN/NX in custody
  - Associated threats/violence
- Over-representation of First Nation (Aboriginal) peoples in custody
  - (~ 8 fold) 3.5% population, 25% in custody

# Understanding NSW Long-acting Opioids in Custody-Treatment (The UNLOC-T study)



- Investigators:

- Adrian Dunlop<sup>1,2</sup>, Jillian Roberts<sup>3</sup>, Nicholas Lintzeris<sup>4,5</sup>, Paul Haber<sup>4,6</sup>, Michelle Cretikos<sup>7</sup>, Judith Mackson<sup>8</sup>, Mark Howard<sup>9</sup>, Terry Murrell<sup>9</sup>, John Attia<sup>2,10</sup>, Chris Oldmeadow<sup>2,10</sup>, Andrew Searles<sup>2,10</sup>, Michael Doyle<sup>4</sup>, Liz McEntyre<sup>11</sup>, Libby Brown<sup>12</sup>

- Research & Clinical Staff

- Bethany White<sup>4,6</sup>, Dena Attalla<sup>3</sup>, Hellal Hussein<sup>3</sup>, Sobi Kim<sup>3</sup>, Monique Hourn<sup>1</sup>, Kerryyn Butler<sup>4,6</sup>, Sophia Little<sup>4,6</sup>

1 Hunter New England Local Health District

2 University of Newcastle

3 Justice Forensic Mental Health Network

4 Discipline of Addiction Medicine, University of Sydney

5 Sydney South East Local Health District

6 Sydney Local Health District

7 Centre for Population Health, NSW Ministry of Health

8 Legal & Regulatory Services Branch, NSW Ministry of Health

9 Corrective Services, NSW Department of Justice

10 Hunter Medical Research Institute

11 Durri Aboriginal Corporation Medical Centre

12 Aboriginal Health Unit, Nepean Blue Mountains Local Health District

- Funding: NSW Ministry of Health
- Medication: depot buprenorphine (CAM 2038 weekly/monthly): Camurus AB  
methadone (Department of Health Australia)

# Study objectives

- Primary:
  - Safety & tolerability of depot buprenorphine in custodial settings
  - Assess diversion and non-medical use of depot buprenorphine
  - Costs of depot buprenorphine (compared to standard care)
- Secondary
  - Retention in treatment, drug use (self report)
  - Patient satisfaction with treatment
  - General physical, mental health, psychosocial functioning
  - Assess staff satisfaction and acceptability

# Eligibility criteria

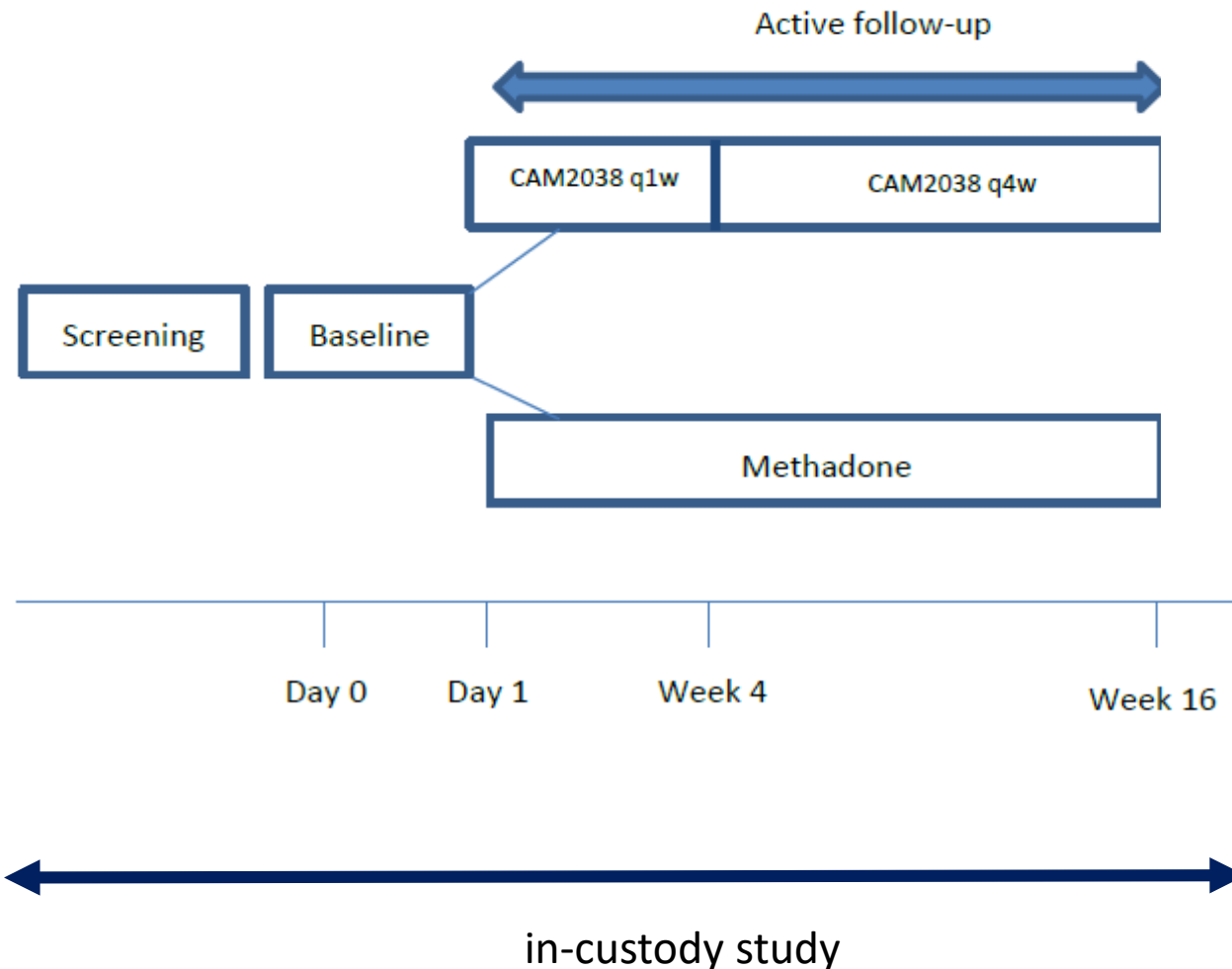
- Inclusion criteria

- Adult (male and female) prisoners ( $\geq 18$  years old)
- Sentenced in full-time custody, with **at least six months** remaining on sentence
- **Moderate to severe Opioid Use Disorder**

- Exclusion criteria

- Unstable **medical / mental health condition/suicidality**
- **Forensic mental health patient** not guilty by reason of mental illness
- Currently **breastfeeding or pregnant**
- **Enrolled in a residential or intensive treatment program** (Intensive Sex Offender Treatment Program, Compulsory Drug Treatment Program and Drug Court Program)

# Study design



- Two-arm, case-comparison study (non randomized)
  - Methadone: Standard care, already stable on methadone
  - Depot BPN: Opioid dependent, not currently on methadone/ buprenorphine treatment
- Sites:
  - 7 prisons across NSW
  - Mix of metro/rural, security levels, female & male

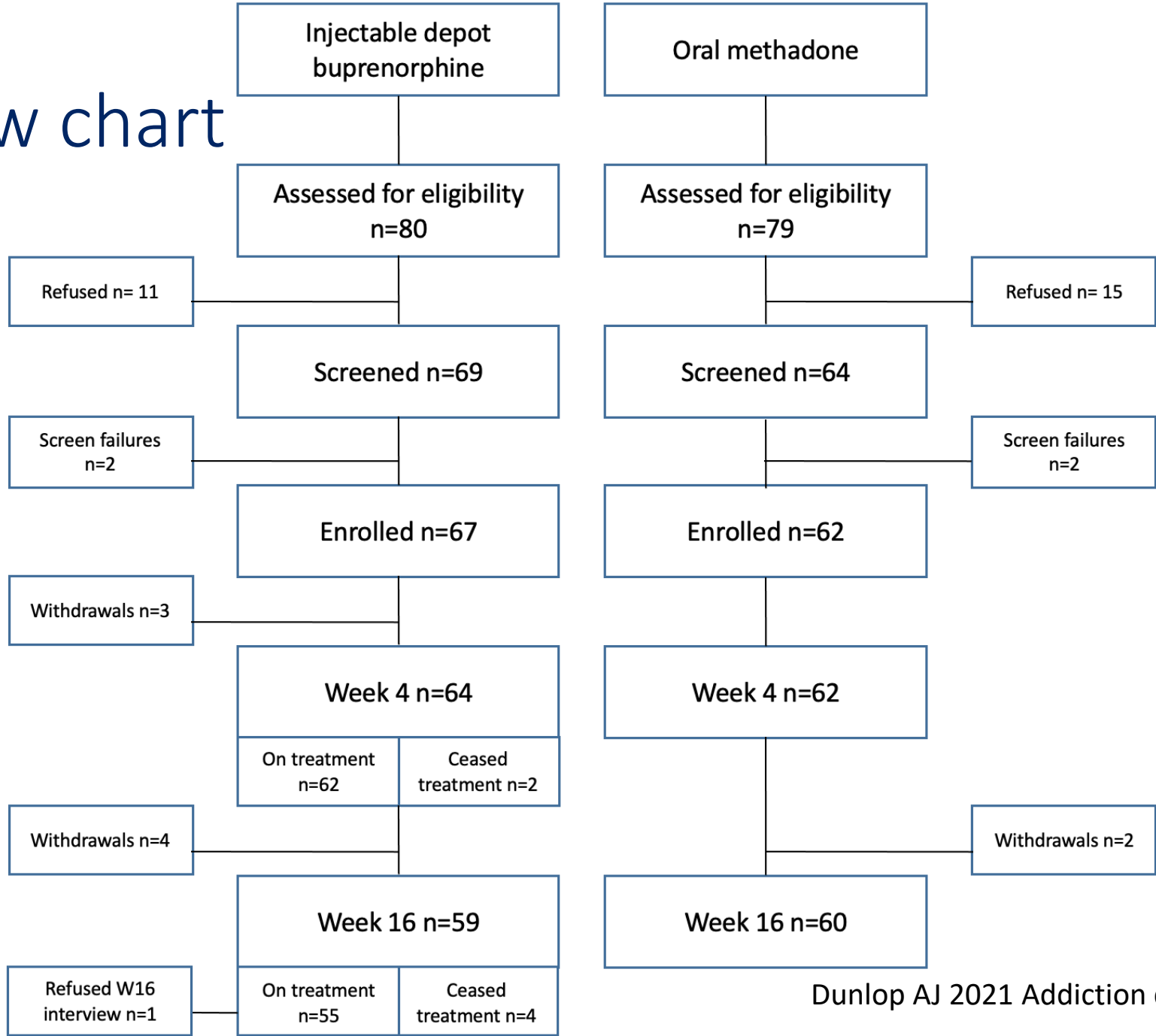


# Medication – flexible doses

- Methadone: standard care
  - Typically - >80 mg
- Buprenorphine
  - Suboxone (buprenorphine-naloxone SL film)
    - 4 mg day one ('test' dose) - tolerance test
  - Buvidal (depot-BPN)
    - 4 x weekly (weeks 1-4)
      - 16mg weeks 1-4, may be titrated up (24mg, 32 mg doses)
    - 3 x monthly (weeks 5-16)
      - 96 mg, may be titrated up or down (64mg, 128mg, 160mg doses)



# Study flow chart



# Demographics baseline & clinical characteristics

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Characteristic	Depot BPN n=67	Methadone n= 62	<i>p</i>
Age, years, mean (SD)	34 (7.5)	38 (8.9)	0.004
Male (%)	82%	86%	0.602
Australian born (%)	94%	94%	0.910
Aboriginal and/or Torres Strait Islander (%)	45%	34%	0.206
Did not complete high school (%)	48%	68%	0.014
BMI, kg/m <sup>2</sup> , mean (SD)	28.7 (5.6)	30.7 (7.7)	0.046

# Demographics baseline & clinical characteristics

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Characteristic	Depot BPN n=67	Methadone n= 62	<i>p</i>
Anti-HCV + (%)	76%	84%	0.273
Of those anti-HCV+, HCV RNA detected (%)	31%	4%	<0.001
Previous OAT (%)	70%	97%	<0.001
Mean number previous OAT episodes (SD)	1.6 (1.9)	2.4 (1.8)	0.027
Baseline methadone dose (mg), mean (SD)	NA	92.7 (38.0)	-
Ever overdosed on opioids (%)	37%	52%	0.102
Subjective opioid withdrawal scale (SOWS), mean (SD)	3.7 (5.5)	2.8 (5.3)	0.341
Opioid craving; need-to-use VAS, mean (SD)	52.9 (32.4)	18.4 (23.0)	<0.001

## Summary of treatment related adverse events in depot BPN patients

Category	Depot BPN n= 67 (%)
≥ 1 TEAE	65 (97)
≥ 1 Drug-related TEAE	63 (94)
• Injection site reaction (≥ 2 mild or ≥ 1 moderate injection-related AEs)	14 (12)
• Non-injection site AE	56 (84)
Deaths	0
≥ 1 Serious Adverse Event	2 (3)
• Hospital admission	2 (3)
Drug-related AE leading to discontinuation	4 (6)*
Overdose	0

\*2 clinician-observed, 2 self-reported

# Summary of treatment related adverse events in depot BPN patients-

Drug-related TEAE in > 10 % of depot BPN participants	n= 67 (%)	Severity n = 67 (%)		
		Mild	Moderate	Severe
Injection site pain	34 (51)*	35 (52)	1 (2)	0
Constipation	34 (51)*	26 (39)	9 (13)	0
Injection site swelling*	23 (34)	22 (33)	1 (2)	0
Headache	19 (28)*	16 (24)	4 (6)	0
Injection site erythema	15 (22)	15 (22)	0	0
Nausea	14 (21)	13 (19)	1 (2)	0
Vomiting	13 (19)	10 (15)	3 (4)	0
Self report sedation	10 (15)*	10 (15)	1 (2)	0
Self report urinary hesitancy	12 (18)	9 (13)	1 (2)	0
Pruritus	7 (10)	7 (10)	0	0
Rash	7 (10)	6 (9)	1 (2)	0

\*Includes induration

# SAE: Acute hepatitis during depot buprenorphine induction

- 36 year old male. Reinfection HCV x 3 (spontaneously cleared x2, DAA x1 in 2018 with SVR). Anxiety/ depression/ PTSD on Mirtazapine 30mg
- Reported ~32mg/day IVDU of illicit buprenorphine-naloxone for >8 years prior. Previous methadone program in 2007 for 6/12. Assessed for induction onto CAM2038 - UNLOCT
- **SCREENING:** HCV PCR +ve, nil genotype (viral load too low: 4.54E+1 IU/mL), ALT 92, GGT 91, all else NAD. **INDUCTION:** 4mg SL SBX, 2x weekly depot (16mg, 24mg)
- **PROGRESS:** Ongoing IVDU of illicit buprenorphine-naloxone reported, + on the day 3rd weekly depot due, patient unwell: T39.8°C, icteric, RUQ pain, dark urine, so DOSE WITHHELD
- Sent to ED. ED investigations: ALT 3905, AST 2742, GGT 177, ALP 205, SBR 100, INR 1.3, CRP 63, HCV PCR +ve, viral load 1.73E+3 IU/mL (↑ from screening), ANA +ves speckled 1:160 titre, RF +ve20, Anti-CCP -ve, GFR >90. Abdo-CT peri-cholecystic fluid with NO stones. Nil objective opioid withdrawal in hospital.
- **OUTCOME:** Transferred to methadone 1/52 later (since lack of safety data RE: continued depot buprenorphine during severe acute HCV). LFTs normalised, HCV spontaneously cleared 1/12 later

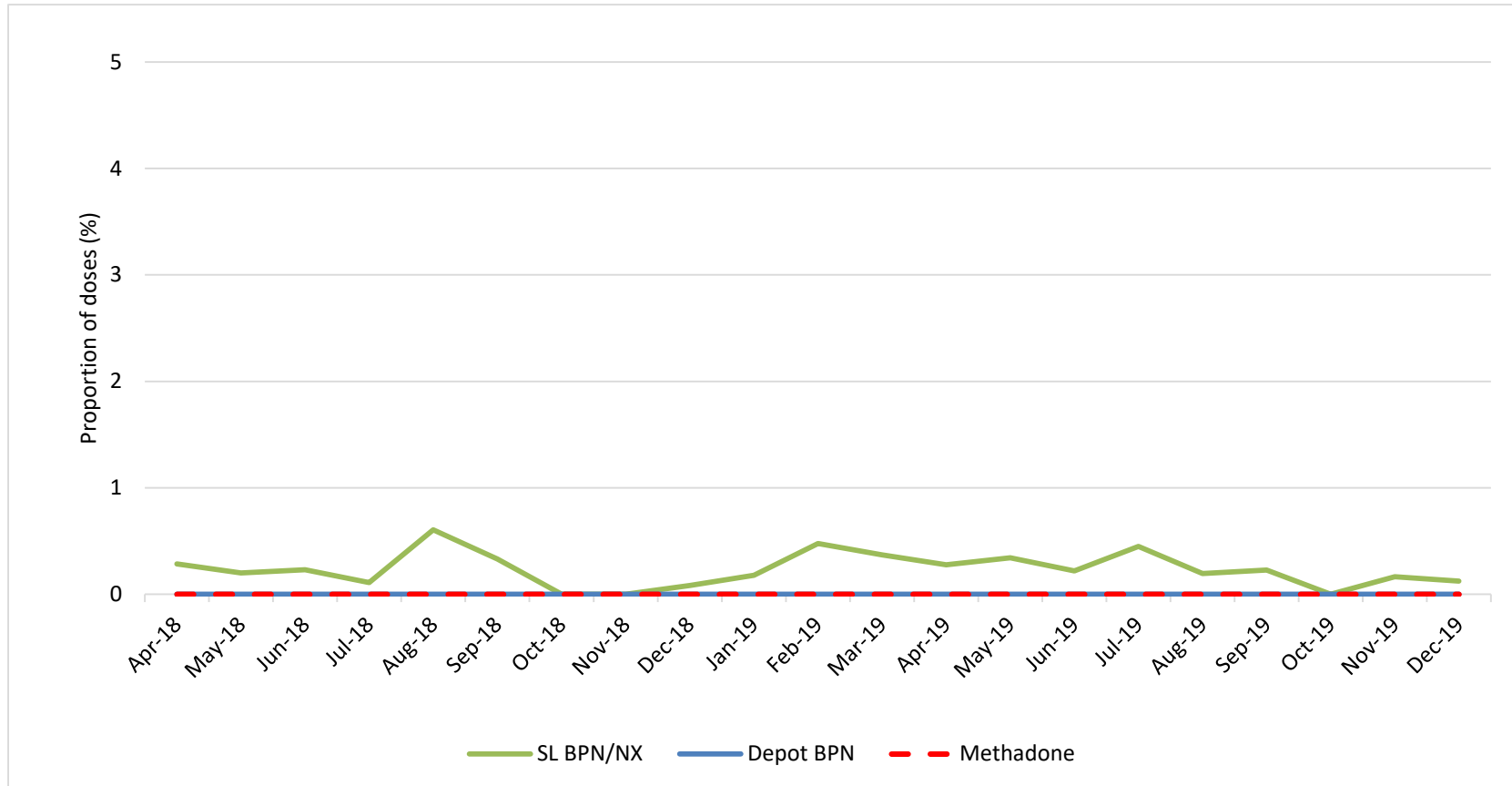
# SAE: Acute hepatitis during depot buprenorphine induction

## CONCLUSION

- Despite history of prescribed depot buprenorphine + illicit IV buprenorphine-naloxone, hepatologist opinion was that ↑ LFTs were not caused by buprenorphine and most likely cause was severe acute HCV (viral load ↑ from pre-induction level)
- Further clinical experience may support ongoing treatment with SL and/or depot buprenorphine in cases of severe acute HCV.



# Medication diversion



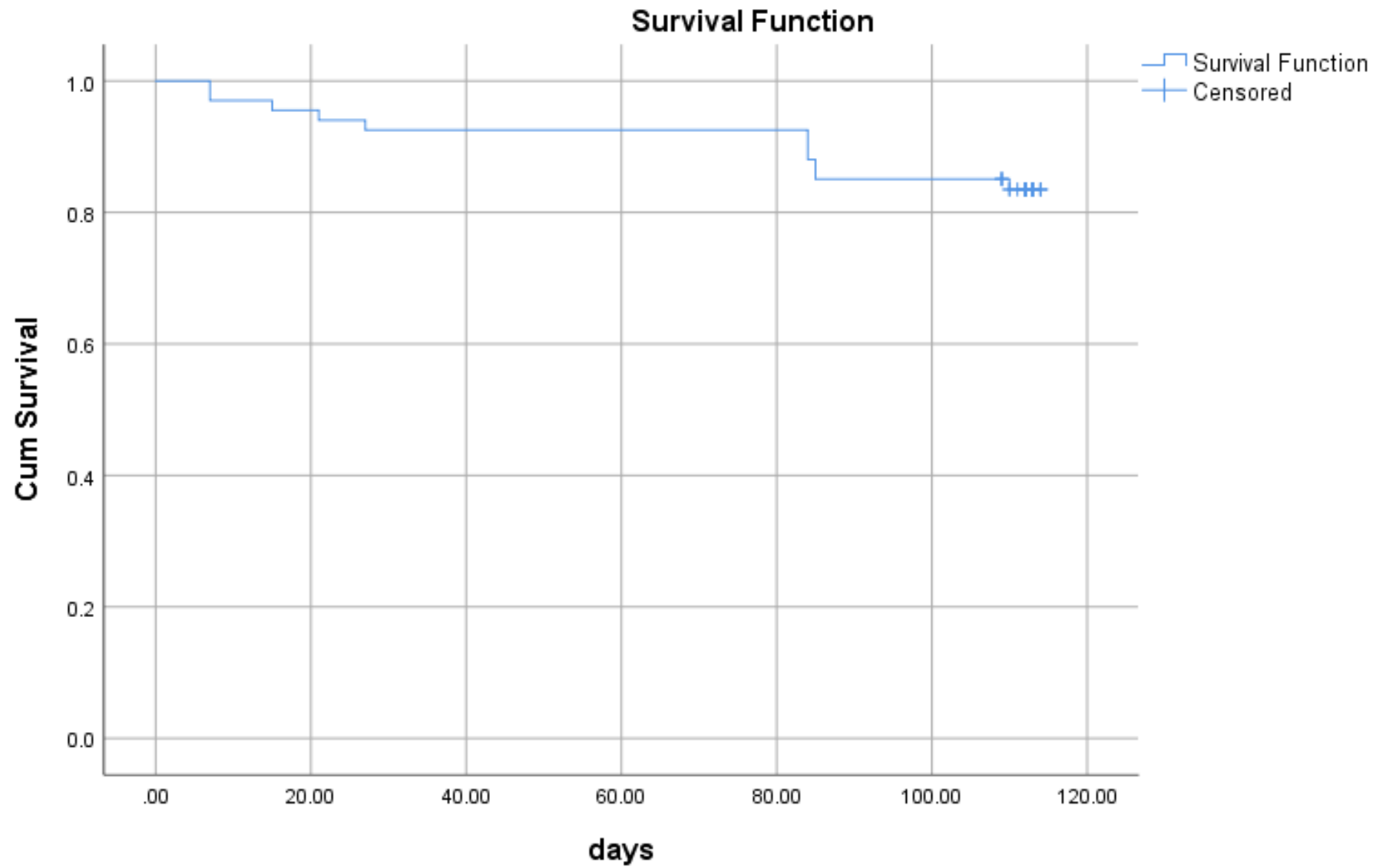
- No observed or self-reported diversion of depot BPN or methadone
- No evidence of diversion (examination of depot injection sites) of depot-BPN

Proportion of depot BPN doses, methadone and SL BPN doses diverted at UNLOC-T trial sites, JHFMHN incident data

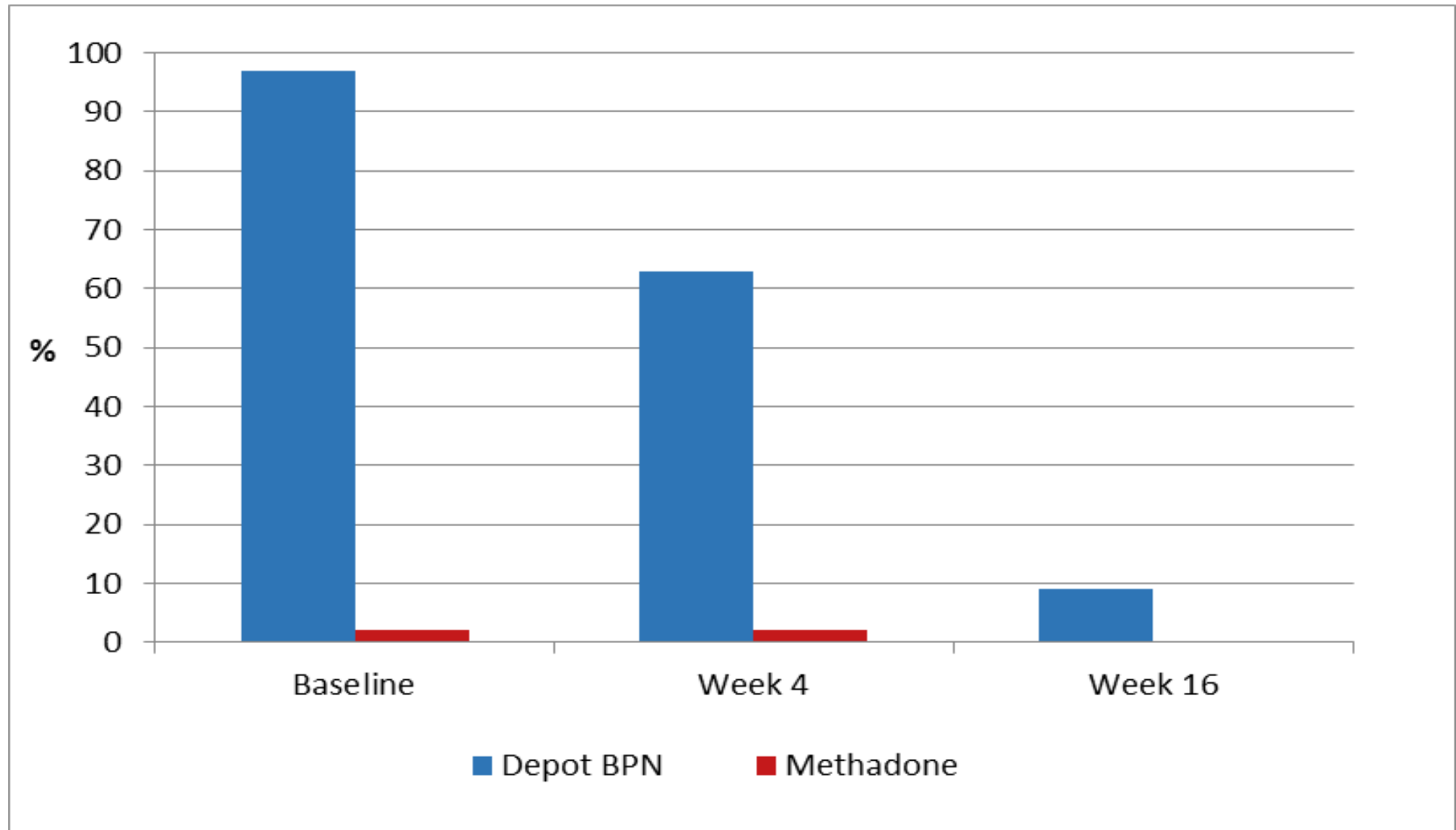
# Treatment costs – \$AUD

	Depot BPN	Methadone	SBL BPN
<b>Justice Health &amp; Forensic Mental Health</b>			
Pharmacy	\$23	\$4	\$30
Inventory management	\$24	\$4	\$16
Clinic OAT administrations	\$46	\$198	\$838
Total	\$94	\$206	\$884
<b>Corrective Services NSW</b>			
Movement Supervision	\$31	\$68	\$303
Clinic Supervision	\$19	\$86	\$287
Total	\$50	\$154	\$590
<b>Total NSW Government (\$)</b>	<b>\$143</b>	<b>\$361</b>	<b>\$1,474</b>
Patients (n)	50	239	40
Administrations (n)	84	7,409	1,240
Orders to Pharmacy (n)	0	21	24
<b>Commonwealth Government</b>			
OAT supply costs per patient	<b>\$434</b>	<b>\$80</b>	<b>\$525</b>

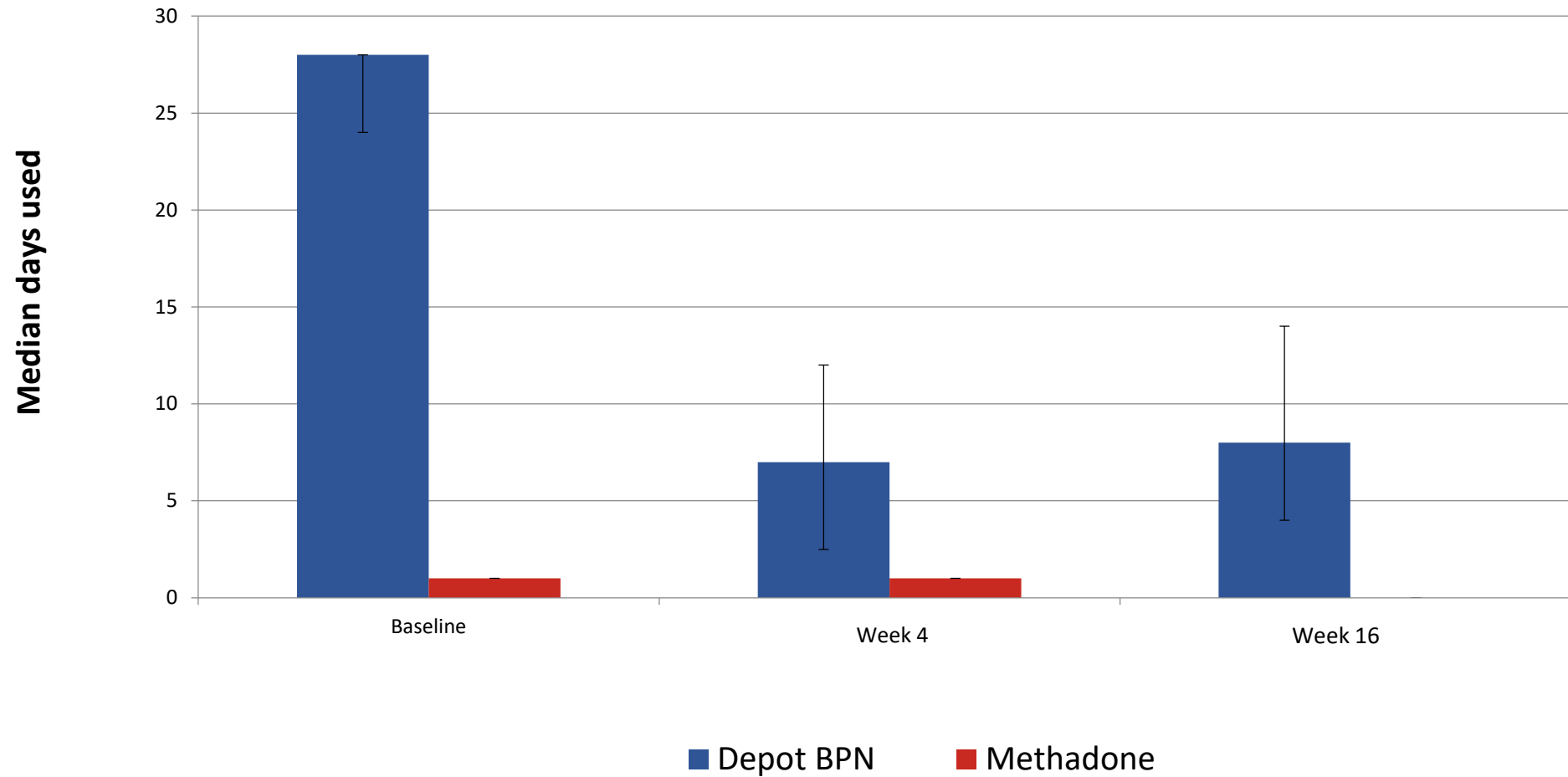
Retention  
in depot  
BPN  
treatment



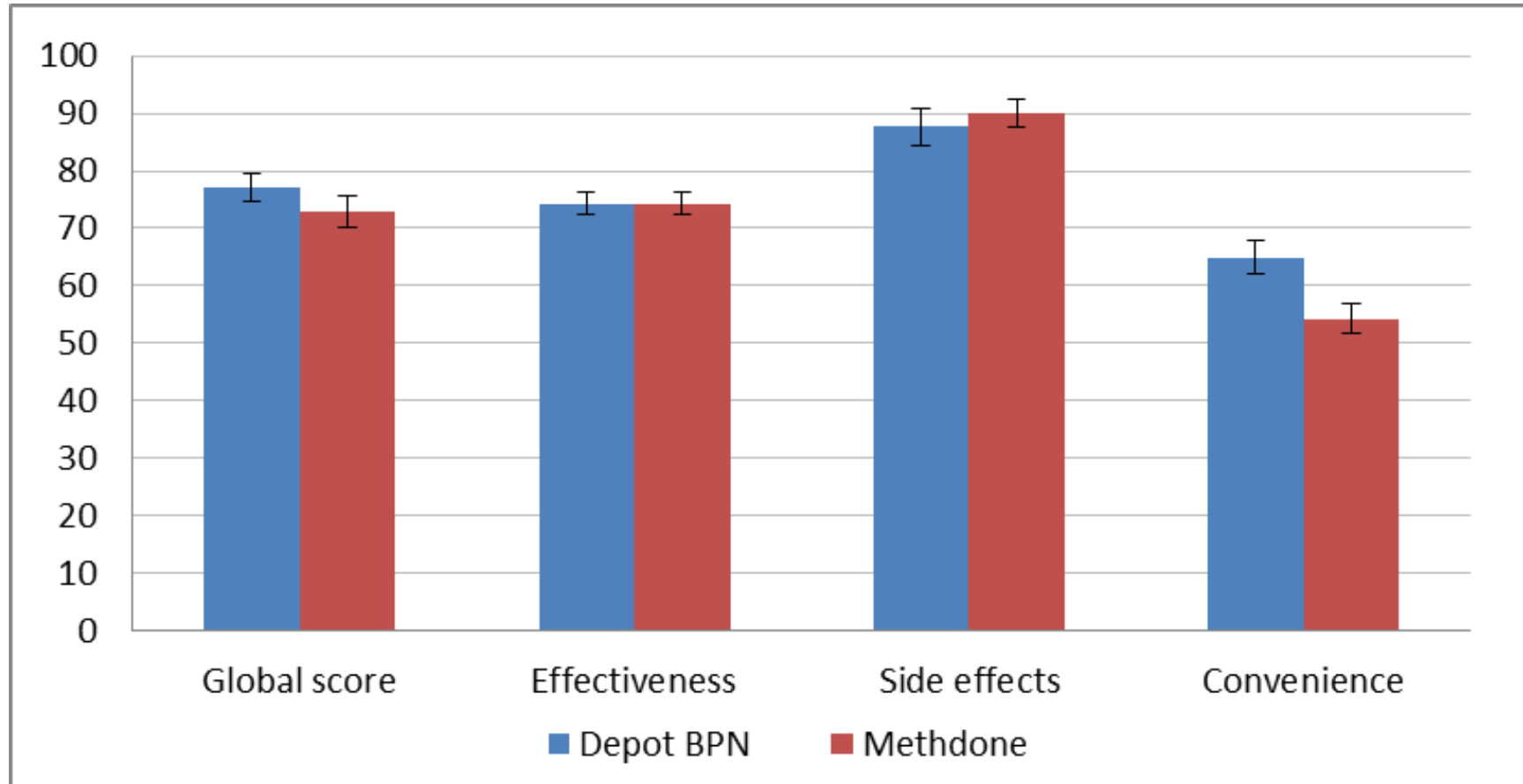
# Prevalence of self-reported non-prescribed opioid use last 28 days- depot and methadone patients



# Frequency of self-reported non-prescribed opioid use last 28 days- depot and methadone patients, median (IQR)



## Treatment Satisfaction Questionnaire for Medication (TSQM) – Week 16



At Week 16 depot patients scored significantly higher (higher score= greater satisfaction) in the convenience domain of the TSQM compared to methadone patients ( $p=0.01$ )

# Clinical experience..

I feel like  
Santa Claus

Wonderful to see  
patients walking in  
with smiles on their  
faces



I have best job in the  
world seeing these  
fellas do so well

Game  
changer

# Clinical experience..

CSNSW -Commissioner,  
General Managers and  
Clinic Officers very  
supportive



Management are  
aware of the trial,  
know that we have  
more stability,  
giving us more  
responsibility

We wake up and  
don't have to think  
about how to score

When I get home I can  
do my job as a builder  
because I don't need to  
go to clinic everyday

Not even on  
same spectrum  
as methadone



Don't have to  
worry about  
standover



# Conclusions

- No subjective/objective evidence of diversion of depot-BPN during study
- Adverse events: common, mild in severity
- Retention: acceptable (81% 16 weeks)
- Drug use: (self report) decreased illicit opioid use in depot-BPN group over study – started to resemble a stable comparator (methadone)
- Costs: depot-BPN ~1/3 methadone, 1/10 SL BPN/NX
- Greater awareness of the extent of non-prescribed SL BPN use in custody

## Treatment of opioid dependence with depot buprenorphine (CAM2038) in custodial settings

Adrian J. Dunlop<sup>1,2,3</sup> , Bethany White<sup>3,4,5</sup> , Jillian Roberts<sup>3,6</sup> , Michelle Cretikos<sup>7</sup>, Dena Attalla<sup>6</sup>, Rod Ling<sup>8</sup> , Andrew Searles<sup>8</sup> , Judith Mackson<sup>9</sup>, Michael F. Doyle<sup>4,10</sup> , Elizabeth McEntyre<sup>11</sup>, John Attia<sup>2,8,12</sup> , Christopher Oldmeadow<sup>8</sup> , Mark V. Howard<sup>13</sup>, Terry Murrell<sup>13</sup>, Paul Steven Haber<sup>3,4,5</sup>  & Nicholas Lintzeris<sup>3,5,14</sup> 

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Dunlop AJ, White B, Roberts J, Cretikos M, Attalla D, Ling R, Searles A, Mackson J, Doyle MF, McEntyre E, Attia J. Treatment of opioid dependence with depot buprenorphine (CAM2038) in custodial settings. *Addiction*. 2021 doi:10.1111/add.15627

# Other impacts

- Positive momentum from patients, health staff, corrective services.  
Peer to peer positive stories
  - Operational changes - patient focused staff skilled at trouble shooting barriers- “can do” attitude
- Mid 2019 preparing upscaling depot BPN treatment as soon PBS listing (9/2019)
- **Immediate commencement of translation into practice!**
  - Transitional grant for JHFMHN – NSW Health
  - The Covid-19

# Covid-19 and NSW prisons

- Significant concern regarding risks of spread of SARS Cov-2 in prisons
- Droplet spread – concerns re dosing OAT
  - Challenges in dosing people in isolation
- **Parole** utilized – 10% decrease in total numbers in custody
- **Visits stopped** – 19/3/20
- Rapid increase in demand for SL BPN
  - Several riots, serious incidents
  - Illicit cost \$1k for 8mg film



No visits, no drugs: Prison riots during COVID lockdown

**Inmates charged over Cessnock prison riot, Sydney jail records state's first COVID-19 case**

ABC Newcastle / By Giselle Wakatama

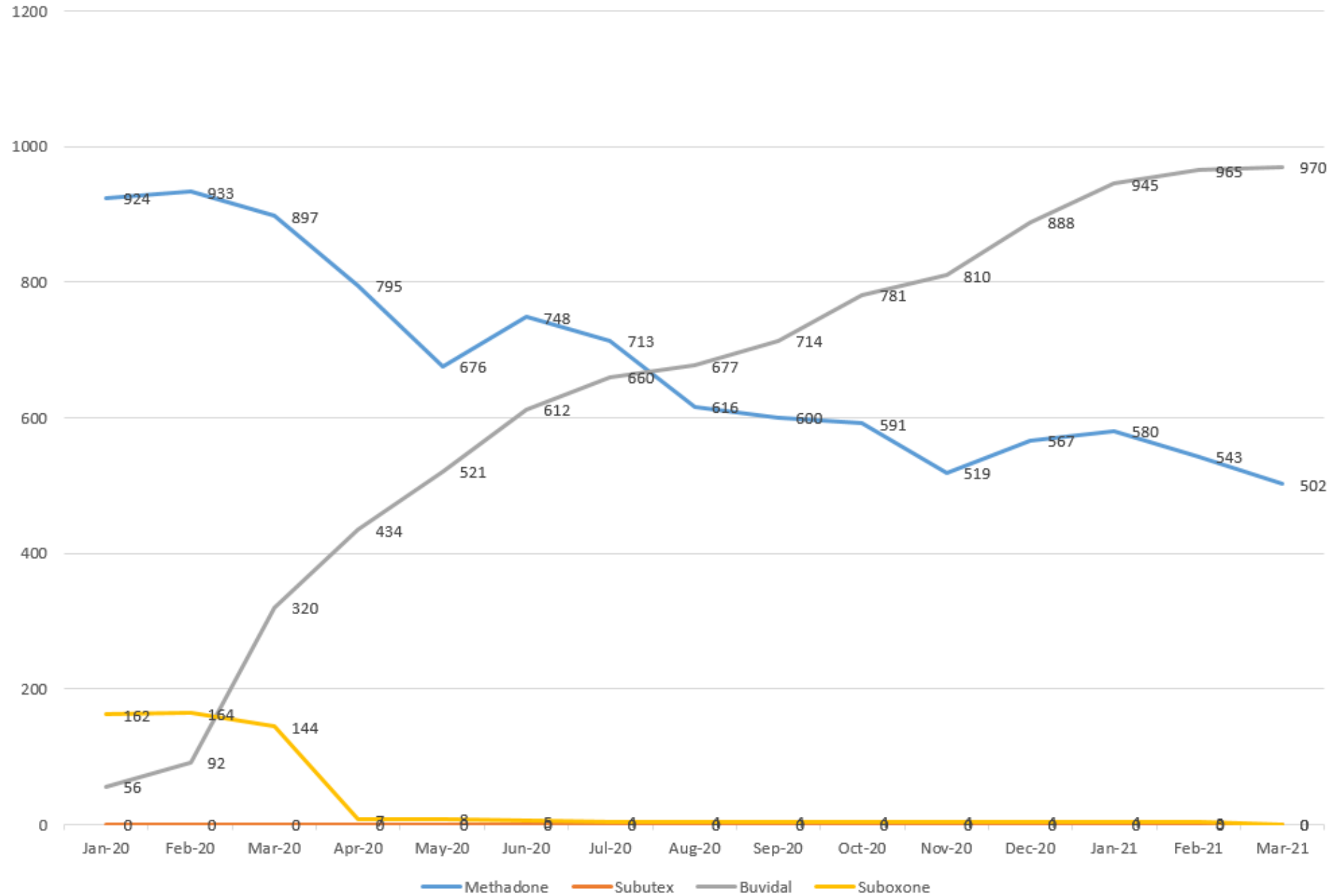
**Prisons see violence spike as isolation cuts drugs supply**

By Ben Millington on AM

APRIL 30 2020 - 2:13PM

**Prisoners riot at Cessnock jail, lock themselves in rooms, reportedly light fires**

OAT Patients in JHFMHN Facilities



# Release study



Drug & Alcohol Clinical Research & Improvement Network

- NSW TRGS funded cohort study 2021-2023
- Investigators: A Dunlop, J Roberts, P Haber, N Lintzeris, R Graham, N Ezard, L Maher, E McEntyre, B White, M Doyle, M Nean, B Lokuge, K Kypri, M Sequeira, C Oldmeadow, A Searles, C Jorm
- People released from custody from NSW correctional centres to DACRIN – LHDs (SSE, S, StVs, WS, SWS, IS, CC, HNE, JH&FMHN)
- Comparison of patients released on methadone and depot BPN
- Outcomes
  - Retention in treatment – 3 months
  - Substance use, return to prison, mental health, overdose, ED, hospitalisations, death
  - Co-variates: support post release, planned/unplanned release, rurality, traineeships in custody, take home naloxone access