CESPHN Webinar

Using opioid agonist treatment for pharmaceutical opioid dependence
Acknowledgements

This webinar was produced for Central and Eastern Sydney Primary Health Network

Drug and Alcohol support for service providers

Central and Eastern Sydney PHN is funded to ensure an integrated regional approach to drug and alcohol services by developing evidence-based plans and service mapping that identify needs and gaps, increase efficiencies and encourage easier access to and increased referral pathways to drug and alcohol services and supports.

This website provides tools and resources to help you navigate the drug and alcohol treatment service sector and find assistance that supports your needs.

Resources and links

Online and phone assistance

Face-to-face services

Emergency or crisis?
Learning objectives

1. Understand the prevalence of dependence to pharmaceutical opioids (PO)
2. Be familiar with the evidence for the use of opioid agonist treatments for PO dependence
3. Understand dose requirements for opioid agonists
4. Be familiar with safety considerations with the use of opioid agonist treatments
Introducing Olga

- Olga is a 49yo women with a 15 year history of codeine use (OTC and prescribed)
- Started using for headaches, increased to daily use within a few years
- Escalated during separation from partner
- Taking 45-60 tablets daily (mainly ibuprofen codeine) +/- paracetamol-codeine prescribed
- Recent duodenal haemorrhage and anaemia
- More difficulty accessing codeine (prescribed and OTC), has come to you asking for help
Prevalence of Dependence to Pharmaceutical Opioids
Most commonly used opioids in Australia

Chronic pain and opioid use disorders

Systematic review: Rates of ‘addiction’ averaged between 8% and 12% (range, 95% CI: 3%-17%)

Pain and Opioids IN Treatment (POINT) cohort – Australian community-based cohort of people prescribed opioids for chronic pain

- One in four (24%) meet criteria for ‘addiction’ ‘behaviour including one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and cravings’
- One in five (18.6%) met lifetime criteria for ICD-10 PO use disorder
- Almost one in ten (9%) meet criteria for ICD-10 PO dependence (19% meet ICD-11 definition for dependence)


Campbell, Nielsen, Larance et al (2015). Pharmaceutical opioid use and dependence among people living with chronic pain: Associations observed within the Pain and Opioids IN Treatment (POINT) cohort. Pain medicine, 16(9), 1745-1758.

Those on the highest doses report the most problems AND report less pain relief (compared to lower doses)


% lifetime ICD-10 pharmaceutical opioid dependence
% lifetime ICD-10 harmful pharmaceutical opioid use
% at least some non-adherence, past 3 months
% intermediate-high (>8) score on the PODS
‘Adverse selection’

- Those with the most complex histories, and therefore with the most risk factors, are prescribed the highest doses
  - Participants with better socio-economic status indicators (income and education, private health insurance, employment) were less likely to be on longer-term opioid analgesic treatment
  - Those with poorer health (smoking, obesity and low physical activity levels) were more likely to receive subsequent opioid analgesic treatment.
  - Those with mental health problems and substance use disorders more likely to receive opioids for pain


Over-the-counter codeine dependence

• Different studies (convenience samples) find approximately one in five people using OTC codeine meet dependence criteria
• No difference on demographic characteristics (age, gender, employment, education) between those that met criteria for dependence and those that do not
• Those meeting dependence criteria more likely to have chronic pain, psychological distress and a history of AOD problems
  o Note – most (58%) people meeting criteria of AOD problems did not have an AOD history
• Most people (75%) that met criteria for dependence had never sought any help

Pharmaceutical opioid dependence: Increasing treatment demand

- One in three* people in OST (*where opioid type reported) report a PO as the main drug at treatment entry

- Among people entering OST (methadone and buprenorphine+/- naloxone) increasing numbers report codeine as the main drug
  - 2014 – 2.7% of cases (1287 people)
  - 2015 – 3.5% of cases (1676 people)
  - 2016 – 4.6% of cases (1562 people*)

* missing data from Vic and ACT means actual number likely to be higher (>2000)

What is opioid dependence?

Different definitions: DSM IV-TR
≥ 3 occurring at any time in the same 12 month period:

1. Tolerance
2. Withdrawal
3. Opioids taken in larger amounts or longer than intended.
4. Persistent desire or unsuccessful attempts to cut down or control use.
5. A great deal of time is spent in activities necessary to obtain opioids, use opioids, or recover from their effects.
6. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
7. Opioid use is continued despite knowledge of harms caused or exacerbated by opioids.
Substance use disorder (DSM-5)

Also considers craving, persistent social problems from use, use in hazardous situations

Severity depends on # of symptom criteria endorsed

Mild: 2-3 symptoms
Moderate: 4-5 symptoms
Severe: 6 or more symptoms
Definitions of opioid dependence ICD-10
(3 or more in 12 months)

Criteria include:

- developing tolerance
- experiencing withdrawal symptoms
- taking more opioids than intended
- unsuccessful attempts to cut-down use
- spending a lot of time obtaining opioids and forgoing important activities because of opioid use
- continuing to use opioids despite knowing the harmful effects
Characteristics of people who are dependent on pharmaceutical opioids
Codeine dependence (summary)

- Higher proportions of females (50-80%)
  - Increasing numbers of young makes seeking treatment
- More commonly employed
- Often commenced for an acute pain condition
- Ongoing use often driven by psychosocial stressors
- Some patients with history of alcohol / benzodiazepine use, less commonly illicit drug use
- Differing use patterns (e.g. high dose, therapeutic dependence)
- Commonly identified secondary to severe harm from taking large doses of ibuprofen and paracetamol
Dependence on prescribed opioids

**Chronic Pain cohort**

10-25% ‘addicted’/dependent
Rarely report non-medical sources
Virtually no heroin use or history of injection
One in three report BZD
One in three report alcohol use disorders
Half meet criteria for moderate to severe depression
One in five have attempted suicide

**PO Treatment Cohort (NSW)**

~40% report chronic pain
Two thirds report commencing pharmaceutical opioids for pain
4 in 10 report medical source for use when problems began
Around 6 in 10 report lifetime heroin use or history of injection
Most (80%) report trauma
Half meet criteria for moderate to severe depression
4 in 10 report moderate to severe anxiety
60% report suicidal thoughts

POINT Pain and Opioids in Treatment Cohort (n = 1514)
Pharmaceutical Opioids Treatment Cohort (n = 108)
Treatment options
Opioid agonist treatment

OST will not be appropriate for all patients that experience problems with pharmaceutical opioids ..so which patients?

OST may be appropriate where:

- Confirmed opioid dependence (ICD-10)
- Attempts to manage opioids with other strategies failed (+/- taper unsuccessful)
- Risk of overdose / relapse
- Patient willing to consider OST
Why examine the evidence for pharmaceutical opioid dependence?

- **Reasons to explore:**
  - Most research using opioid agonist treatments examined people who use heroin
  - Important differences in co-morbidities (e.g. more severe pain and mental health) may impact on treatment outcomes

→ Treatment needs and outcomes may not be assumed from research on people who are dependent on heroin
Methadone and buprenorphine

Methadone: oral liquid, full opioid agonist

Buprenorphine: usually combined with naloxone (to reduce injection), sublingual film or tablets, partial opioid agonist
Full and partial agonists

- **Full agonist** (e.g. morphine, heroin, methadone)
- **Partial agonist** (e.g. buprenorphine)
- **Antagonist** (e.g. naltrexone, naloxone)

Increasing dose

Threshold for fatal respiratory depression
Evidence for taper (detox) v maintenance

Advantages of detoxification

→ Entry point for treatment for those unwilling to enter long term treatment
→ Shorter-term commitment (more flexible)

Disadvantages

→ Typically low success rates e.g. PO dependence: 91-93% has ‘unsuccessful outcome’ with 2 or 12 weeks of treatment
→ Not appropriate as standalone treatment
→ Increased overdose risk


Weiss R, et al. (2011) A Two-Phase Randomized Controlled Trial of Adjunctive Counseling during Brief and Extended Buprenorphine-Naloxone Treatment for Prescription Opioid Dependence. Arch Gen Psychiatry
Retention and substance use outcomes are better with longer-term (i.e. maintenance treatments) compared to short-term taper or psychological interventions only

- Includes when substance use outcomes are measured with urine drug screens or self-report
- Based on three RCTs with 206 people

“Low quality evidence (small studies) suggests that most patients will have better outcomes with longer-term treatment”

Cochrane review: Methadone versus buprenorphine

Three RCTs, 360 patients

- No difference in retention outcomes
- No difference in substance use outcomes
- Other factors such as patient preference, safety and unsupervised dosing options may inform decision

Opioid agonist treatment for pharmaceutical opioid dependent people (Review)

Nielsen S, Larance B, Degenhardt L, Gowing L, Kehler C, Lintzeris N
Other aspects of treatment:

Induction
Dose
Predictors of treatment outcomes
Psychosocial treatment
Induction onto pharmacotherapy

Methadone

- ‘Start low, go slow’ – risk of toxicity, accumulation or misjudging level of neuroadaptation can lead to overdose
- Usually 20-30mg starting doses, never more than 40mg, lower doses with polydrug use or unclear level of dependence
- Monitor for sedation

Buprenorphine

- Less respiratory depression that with methadone
- Don’t start until observable opioid withdrawal symptoms (sweating, dilated pupils, stomach cramps, muscle pain etc) – risk is with precipitated withdrawal
- Test dose of 2-4mg, additional dose if required after 1-2 hours
Precipitating Acute Withdrawal

- If buprenorphine is administered while opioids still active it may precipitate withdrawal when it displaces the full agonist off the mu receptors.
Buprenorphine induction

Buprenorphine: Getting to the right dose and avoiding precipitated withdrawal

Studies examining occurrence of precipitated withdrawal found no difference between:

- pharmaceutical opioids and heroin
- different pharmaceutical opioids

 Nb. These studies used standard protocols (i.e. start buprenorphine when in mild withdrawal, defined duration from last opioid dose until first buprenorphine dose)

→ Lower ratings of opioid withdrawal prior to buprenorphine was associated with greater risk of precipitated withdrawal


Buprenorphine treatment for codeine dependence

• Codeine is considered a ‘weak’ opioid
  Standard induction procedures
• Dose requirements consistent with ‘strong opioids’ (12-16mg daily) (BPN patch insufficient)
• Considerable variation between patients
Buprenorphine dose: codeine dependence

Lots of individual variation = dose titration

a Buprenorphine dose day 7

b Buprenorphine dose day 28 of treatment

Treating codeine dependence with buprenorphine: Dose requirements and induction outcomes from a retrospective case series in New South Wales, Australia
Predictors of treatment outcomes: heroin use

In buprenorphine taper and long-term treatment studies

→ *Any heroin use* associated with poorer outcomes (more opioid use, poorer retention)

Weiss, et al. (2011) A Two-Phase Randomized Controlled Trial of Adjunctive Counseling during Brief and Extended Buprenorphine-Naloxone Treatment for Prescription Opioid Dependence. Arch Gen Psychiatry.


Predictors of treatment outcomes: pain

Mixed findings:
A study of 2 and 12 week buprenorphine treatment found no difference in outcome by pain status at baseline
A separate examined effect of pain on taper outcomes;
  - Those with moderate to severe pain did better DURING treatment
  - Those with pain had more self-reported use at follow-up (no difference in UDS)

*Note that these studies specifically excluded patients with significant pain that needed opioids for management

One small RCT showed both methadone and buprenorphine resulted in meaningful reductions in pain (patients with chronic pain and opioid dependence)

Open label, retrospective reports of patients transferring from full opioid agonists (e.g. oxycodone) to buprenorphine

- Reduced self-reported pain report after transfer to buprenorphine
- Mean doses of 8–28 mg per day (dose frequency not reported)
- Patients on high opioid doses (> 200 mg OME a day) show comparable or greater improvements in pain and quality of life after transfer

Neuman et al, J Addict Dis 2013
Malinoff et al. American Journal of Therapeutics. 2005
Psychosocial adjunct treatment with OAT

- Fewer studies overall have examined this, mixed findings → important area for more work (esp. for those with pain and dependence)
  - No difference between ‘extended counselling’ (45-60 minutes twice a week) to ‘standard medical management’ (15-20min weekly) in improving abstinence in PO dependent people prescribed buprenorphine
  - Later (smaller) study found PO dependent people may have better outcomes with psychosocial adjunct treatments (e.g. CBT), compared with those primarily using heroin in the same study
- In chronic pain treatment the role of CBT and other behavioural therapies well established

Weiss et al. (2011) A Two-Phase Randomized Controlled Trial of Adjunctive Counseling during Brief and Extended Buprenorphine-Naloxone Treatment for Prescription Opioid Dependence. Arch Gen Psychiatry.
Safety consideration with opioid agonist treatments
High-risk periods with opioid use

Induction onto treatment (first two weeks, especially with methadone)
Cessation of treatment
Change in tolerance (e.g. after a period of abstinence)
Change in health status
Periods of concomitant use of other sedatives (e.g. alcohol, benzodiazepines)
Identifying patients that may need additional support from specialist services

- Polysubstance use, unstable opioid use (i.e. presenting intoxicated)
- Unmanaged psychiatric comorbidity
- Diversion
- Chronic pain (significant pain despite stable opioid use)
Naloxone
Naloxone for chronic pain patients

Among chronic pain patients prescribed opioids:

- Most people prescribed opioids for chronic pain would expect, or appreciate being offered naloxone
- Most people prescribed opioids for chronic pain thing take-home naloxone is a ‘good’ or ‘very good’ idea
- Most people prescribed opioids for chronic pain can not identify signs of opioid toxicity

Good opportunity to discuss risks with opioids and educate on safer use

Supplying naloxone

Check existing knowledge about recognising and responding to overdose:

- Opioid overdose can occur with heroin or prescription pain medication.
- Signs include lack of consciousness, blue/grey lips, no breathing or slow and laboured breathing/snoring, no response to sternum rub

In case of suspected opioid overdose:

- Call an ambulance
- Administer naloxone immediately into the upper arm or thigh
- If person not breathing or laboured, slow breathing → place person on their back and start rescue breathing
- If person breathing: place them in recovery position and monitor the breathing
- Repeat naloxone dose after 2-5 minutes if not improved, or earlier if concerned (safer to give more)
Prenoxad
Overdose action plan

OVERDose ACTION PLAN

CHECK FOR DAnger
Uncapped needles, sharp objects, bystanders etc. Make sure the environment is safe

CHECK FOR RESPONSE
Call the person's name. Shake their shoulders vigorously or rub their chest with your knuckles

IF there is no response, or poor response, SEND FOR HELP
Dial 000 and ask for an ambulance

CLEAR THE PERSON'S AIRWAY
Check their breathing. Watch for their chest rising. Look, listen and feel for 2 breaths in 10 seconds.

IF THEY ARE NOT BREATHING or their breathing is slow or abnormal
Put them on their back, clear and open their airway, pinch their nose and give two rescue breaths

IF THEY ARE STILL NOT BREATHING
GIVE NALoxONE
Remove Naloxone mini-jet from package, unscrew the cap and screw on needle.

Inject the entire contents into muscle of the upper arm or thigh and even though clothing in an emergency.

Note the time given.

Continue rescue breathing—1 breath every 5 seconds

IF THERE IS NO RESPONSE
Inject another dose of Naloxone in 2-5 minutes.

Note the time given, continue rescue breathing.

If you are worried give another dose at any time.

If the person is breathing normally, then put them in the recovery position and monitor them. Ensure that their airway is clear and open.

If still no response, commence CPR—30 compressions, then 2 breaths; repeat

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For more information, including a list of organisations that provide training visit: www.credu.edu.au/naloxone
Naloxone administration

Administer in the upper arm or outer thigh
OK to administer through clothes in an emergency
Naloxone has a shorter half-life than many opioids (e.g. heroin, methadone) → stay with the person, call the ambulance – a second dose may be required
Summary of information

- Pharmaceutical opioid dependence is common among those using opioids for pain
- Emerging evidence supports that use of opioid agonist treatment (large evidence base supports opioid agonist treatment in general)
- Dose titration is important, but ‘usual’ doses are common
- Treatment outcomes are comparable/favorable in contrast to treating heroin dependence
  - Existing treatment protocols based on earlier research appear appropriate
More information about opioid agonist treatment

In New South Wales GPs can prescribe buprenorphine for up to five patients without accreditation

- Ideal where a patient already has a good relationship with their GP
- Secondary consultation may support less experienced prescribers, especially around induction

Information about the Opioid Treatment Program:

Opioid Treatment Accreditation Course: https://www.otac.org.au/

National Guidelines:
How to become an OTP registered pharmacy


• Need to register with the NSW Ministry of Health

• May be eligible for the Pharmacy Incentive Scheme
A brief summary of the evidence:

Drug and Alcohol Specialist Advisory Service

For health professionals only:

- advise on clinical diagnosis and management of patients with alcohol and other drug related problems
- available 24 hours a day, 7 days a week.
- FREE

Sydney Metropolitan: (02) 9361 8006
Regional and rural NSW: 1800 023 687

If you are worried about complexities in the patient or person presenting to you, get advice and guidance immediately.
GLAD:

Gp Liaison in Alcohol and other Drugs
To improve collaboration between AOD services and GPs in the CESPHN area
Public alcohol and other drug services
  - SLHD
  - SESLHD
  - St Vincent's Network
  - CESPHN
Our contact michelle.schulz@health.nsw.gov.au
GLAD To seek advice and information

<table>
<thead>
<tr>
<th>Location</th>
<th>Contact Information</th>
<th>Service Requested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sydney Local Health District [RPAH, Concord, Canterbury]</td>
<td>Call RPAH 02 9515 6111</td>
<td>Ask for On Call Drug and Alcohol Doctor</td>
</tr>
<tr>
<td>South East Sydney Local Health District [Sydney, Prince of Wales, St George and Sutherland Hospital’s]</td>
<td>Call Sydney Hospital 02 9382 7111</td>
<td>Ask for On Call Drug and Alcohol Doctor</td>
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<td>St Vincent’s Hospital Network</td>
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24 hour telephone advice and support for patients:

- **ADIS** (Alcohol and Drug Information Service) on **02 9361 8000** for patients to call (website also available).
GLAD: To arrange Referral

If your patient needs specialist drug and alcohol assessment and treatment either as an inpatient or outpatient; Call your local AOD intake team

| Sydney Local Health District [RPAH, Concord, Canterbury] | Call the Centralised Intake Line Intake: 1800 793 466 or 02 9767 8653 Email: SLHD.DHSIntake@sswahs.nsw.gov.au Fax (Camperdown): 95158970 Fax (Concord): 02 9767 8327 | Ask for Drug and Alcohol Intake |
| South East Sydney Local Health District [Sydney, Prince of Wales, St George and Sutherland Hospital’s] | Call Sydney Hospital 02 9382 7111 Fax (Surry Hills-Botany): 02 9332 8700 Fax (St George Area): 02 9113 3977 Fax (Sutherland Area): 02 9540 7097 | Ask for Drug and Alcohol Intake |
| St Vincent’s Hospital Network | Call St Vincent’s Centralised Intake Line Intake: 02 9361 8080 Email: svhs.adsintake@svha.org.au Fax: 02 8382 3111 or Call St Vincent’s Hospital 02 8382 1111 | Ask for Drug and Alcohol Intake |
What happened to Olga?

- Referred to GP, who referred to local Drug Treatment Clinic
- Attended assessment, no interested in opioid agonist treatment
- Tapering trialled, headaches return
- Returns to using ibuprofen-codeine
- Decided to trial buprenorphine-naloxone taper (not ready for longer treatment)
- Stabilised on 12mg daily (twice weekly pick-up),
- Mental Health Care Plan, GP is thinking about taking over prescribing buprenorphine-naloxone
Thank you for being part of this CESPHN-NDARC Webinar

To complete CPD assessment:
https://www.surveys.unsw.edu.au/f/163149/111c/
Open until December 12, 2017
Webinar will be available online at

Questions?