

Frequently asked questions on opioid agonist treatment for pharmaceutical opioid dependence: An evidence summary

This evidence summary comes from a program of work that aimed to build the evidence base for the treatment of pharmaceutical opioid dependence, or dependence on opioid pain medications such as oxycodone, morphine and codeine. Many of the original trials examining methadone and buprenorphine (+/- naloxone) were conducted in people dependent on heroin. In recent years new studies and revised analysis from older studies have aimed to provide information on the use of methadone and buprenorphine (+ naloxone) for those dependent on pharmaceutical opioids such as codeine, morphine and oxycodone. Below is a summary of key findings in a 'frequently asked questions' format. If you have other queries relating this body of research please get in touch at suzanne.nielsen@unsw.edu.au

Q. Can methadone and buprenorphine be used to treatment dependence on pharmaceutical opioids such as codeine or oxycodone?

A. Yes, there is a growing body of smaller studies (1, 2), in addition to a recent Cochrane review (3) that demonstrate that methadone and buprenorphine (+/- naloxone) can be used and are effective in the treatment of pharmaceutical opioid dependence. These medications are generally indicated for the treatment of 'opioid dependence', with no restriction on the type of opioid.

Q. Is methadone or buprenorphine more effective in this population?

A. A Cochrane review compared outcomes for methadone and buprenorphine for people dependent on pharmaceutical opioids. This review found no difference in treatment retention or opioid use between methadone and buprenorphine (3). This suggests that other factors such as patient preferences, stigma issues, logistics of treatment (e.g. access to take-away doses) and potential drug interactions may determine which treatment is most appropriate for an individual patient (4). It should be noted that in general, more research has been conducted with buprenorphine in pharmaceutical opioid dependent populations, which is reflected by more discussion of buprenorphine below, simply because there is more research to discuss.

Q. How long are people who are dependent on pharmaceutical opioid agonists likely to require treatment?

A. Studies of shorter periods of treatment with buprenorphine (2- and 12-weeks of buprenorphine) found almost all people (more than 90%) relapse to opioid use after ceasing buprenorphine treatment (5). Meta-analyses of three studies that compared shorter-term treatments to maintenance pharmacotherapy also found better outcomes in treatment

retention and opioid use with longer-term treatments (3-6 months) (3). This suggests that longer treatment (> 3 months) is likely to be required for most people. This is consistent with the earlier research on treatment of opioid dependence that finds that detoxification alone is rarely effective and treatments of at least 12 months are associated with lower rates of relapse (6, 7).

Q. Do treatment outcomes with opioid agonist treatment differ between pharmaceutical opioid dependent people and heroin dependent people?

A. Studies that have compared these two opioid dependent populations that people dependent on pharmaceutical opioids tend to have more favourable outcomes in terms of retention (i.e. more people stay in treatment) and reduced opioid use (8, 9). These studies have generally compared outcomes in buprenorphine-naloxone treatment between those that were using a pharmaceutical opioid at treatment entry with those using heroin at treatment entry. Studies of prescription opioid dependent people have also found that any history of heroin dependence (even using once in a lifetime) was associated with poorer treatment outcomes, suggesting those who report a history of heroin use may be considered for additional support or more intensive treatment (5, 9).

Q. What evidence is there regarding psychological treatments combined with opioid agonist treatments for pharmaceutical opioid dependent people?

A. One larger study compared additional counseling to standard medical management, and found that the additional counseling did not improve outcomes over standard care (9). It was noted in this study that the standard care platform was of a greater intensity (one or twice weekly visits with the doctor) than usually seen with opioid agonist treatment. A secondary analyses compared a range of psychological adjuncts with buprenorphine+naloxone and found a trend towards better outcomes with those that received CBT, contingency management or a combination of both (9). It should be noted that while not many studies have examined psychological treatments with opioid agonist treatments for those dependent in pharmaceutical opioids, there is a well-established evidence base demonstrating the for those with pain or depression, multimodal treatments including cognitive behavioral therapy and other psychological treatments identified to be important in improving treatment outcomes.

Q. What sorts of doses of methadone or buprenorphine are needed to treat pharmaceutical opioid dependence?

A. The studies we have examined showed that doses of methadone and buprenorphine appear broadly comparable to doses used to treat heroin dependence (1, 2). Interestingly, in a retrospective case series, initial dose of oxycodone or morphine did not seem to be related to dose requirements with methadone or buprenorphine (2). Studies in people dependent on codeine have found that doses of buprenorphine are much higher than might be expected

based on the amount of codeine people were using at treatment entry, though there was a lot of variation between people highlighting that while larger doses are sometimes required, individual titration is important to prevent sedation (1). Larger studies that have compared buprenorphine doses for those dependent on heroin and those dependent on pharmaceutical opioids and found dose requirements did not differ (9), nor did doses requirements differ between different prescription opioids (10). What remains less clear however are the range of effective doses to treat pain and improve pain outcomes. Controlled studies examining the relationship between pain severity or pain interference and different methadone or buprenorphine doses have not been conducted to date.

Q. Do induction outcomes onto buprenorphine vary for different opioids?

A. We compared rates of precipitated withdrawal for prescription opioid dependent people versus heroin dependent people and found they were pretty similar (11). We did find, on average, that those with lower scores for opioid withdrawal doses at induction were more likely to experience precipitated withdrawal (10), highlighting the importance of patients showing objective (physical) signs of opioid withdrawal before the first opioid dose. No difference was found between opioid types for induction outcomes.

Q. What about where patient have chronic pain and opioid dependence?

A. Research examining the effect of pain on treatment outcomes appears mixed. Some find that pain is associated with greater opioid use and others find that those with pain may do better in treatment (5, 12). Importantly, those with chronic pain requiring opioids have been excluded from many higher quality studies (e.g. randomized controlled trials) (5, 12), meaning that we really need more research to inform this area.

Lower quality retrospective reports suggest that for those with chronic pain and opioid dependence, pain may improve after being stabilized on buprenorphine, compared to when patients are on high doses of prescribed opioids such as oxycodone (13, 14).

One small randomized controlled trial with 54 people compared buprenorphine and methadone for those with chronic pain and opioid dependence (15). This study found pain improved in both groups, and did not differ between methadone and buprenorphine treated patients.

There does not seem to be any evidence suggesting that patients with chronic pain cannot be managed well with methadone or buprenorphine (+/- naloxone), however further studies may provide more information on treatment outcomes.

Q. How do I know if opioid agonist treatment is appropriate for my patient?

A. Not all patients' dependent on pharmaceutical opioids may want, or be appropriate for opioid agonist treatment. A detailed assessment of the patient's history, treatment preferences, other treatment options, and potential appropriateness for opioid agonist treatment is required. A summary of the role of opioid agonist treatment is provided here:

<https://www.nps.org.au/australian-prescriber/articles/opioid-treatment-of-opioid-addiction>

Where do I find out more information about prescribing methadone and buprenorphine (+naloxone) in Australia?

There are national guidelines for the use of medication assisted treatment for opioid dependence (4).

<http://www.nationaldrugstrategy.gov.au/internet/drugstrategy/Publishing.nsf/content/ng-mat-op-dep>

Each state or territory has different requirements. Your department of health is a good place to start. Some links are provided below:

Victoria:

<https://www2.health.vic.gov.au/public-health/drugs-and-poisons/pharmacotherapy>

South Australia

<http://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/clinical+resources/clinical+programs/drug+and+alcohol+programs/gp+program+medication+assisted+treatment+for+opioid+dependence>

Western Australia

http://healthywa.wa.gov.au/Articles/N_R/Opioid-pharmacotherapy-in-the-community

Northern Territory

<https://health.nt.gov.au/professionals/environmental-health/medical-practitioners-schedule-8-medicines>

Queensland

<https://www.health.qld.gov.au/clinical-practice/guidelines-procedures/medicines/drugs-of-dependence/qld-opioid-treatment>

New South Wales

<http://www.health.nsw.gov.au/pharmaceutical/doctors/Pages/otp-medical-practitioners.aspx>

Australian Capital Territory

<https://www.health.act.gov.au/sites/default/files/Opioid%20maintenance%20treatment%20guidelines.pdf>

Tasmania

http://www.dhhs.tas.gov.au/mentalhealth/alcohol_and_drug/services/opioid_pharmacotherapy

http://www.dhhs.tas.gov.au/mentalhealth/alcohol_and_drug/publications/statewide_strategy_and_plans/tasmanian_opioid_pharmacotherapy_policy_and_clinical_practice_standards

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