

## 6.2 Methadone shades buprenorphine for outcomes but safety could tip the balance

**Findings** Two meta-analyses combining results from studies comparing sublingual (under the tongue) buprenorphine against oral methadone maintenance for opiate addiction found little difference in retention and illicit opiate use.

In study ① urinalyses from patients retained at the end of nine controlled studies indicated a small, non-significant advantage for methadone. As in study ②, outcomes varied considerably, perhaps partly due to buprenorphine's better performance with patients previously in (presumably unsuccessful) methadone treatment. Study ② took in five of the randomised trials from study ①. To give both drugs the best chance to demonstrate their worth, only the 540 patients given the highest doses in each study (6–12mg daily buprenorphine, 50–80mg methadone) were included. Retention and urinalysis results across the full periods of each study were obtained for each patient. Those on buprenorphine were significantly (26%) more likely to leave treatment early. Excluding a study which tested clearly non-equivalent doses reduced the deficit to 17%, no longer significant. Omitting the same study, whilst in treatment 8% more of the urine tests from buprenorphine patients were positive for illicit opiates, statistically significant. Lower doses of methadone (20–30mg) were less effective than buprenorphine.

LINKS  
Nuggets  
4.6 2.3

**In context** Buprenorphine's advantages derive from its combined opiate and opiate-blocking properties. Overdose is far less likely than on methadone and withdrawal milder. However, it is best taken by the awkward sublingual route and its injectability heightens risk of abuse.

Later trials not included in the featured studies would simply have reinforced their conclusions. The studies' clinical relevance (especially ①) suffered from having to include patients given sub-optimal doses, particularly of buprenorphine. Studies of what is now recognised as bad practice are poor guides to best practice. As with methadone, the number of mg per day is less important than optimising this for each individual even if this means high doses for some. In these circumstances, buprenorphine can perform identically to methadone.

A key issue is buprenorphine's suitability for heavily using addicts who tend to be the prolific offenders from whom treatment reaps cost-savings. Opiate-blocking effects limit the extent to which it can substitute for high doses of heroin and, especially among severely dependent patients, make the start of treatment a high-risk period for drop out.

Though important at the extremes (high dose users, those with severe problems, or whose commitments prevent daily pick up), differences between outcomes on buprenorphine and methadone are small compared to differences between methadone programmes.

**Practice implications** The choice between methadone and buprenorphine should largely be made on grounds of patient preference, how individuals respond, safety and cost, rather than the small difference in overall effectiveness. Buprenorphine is certainly an option for relatively well functioning patients who would otherwise be on moderate doses of methadone. Care is needed to avoid drop-out during induction, especially when patients have been using high doses of heroin or heroin substitutes. Its safety and the feasibility of dosing every two or three days could make it particularly suitable for primary care and for patients resistant to daily visits. Experience in Switzerland commends buprenorphine as a starting and end point for maintenance, with those not held by the drug being transferred to methadone before easing treatment exit by switching back. Concern over misuse by injection and the need for costly supervision to avoid diversion and misuse should be reduced when a buprenorphine/naloxone tablet (ineffective when injected) becomes available.

**Featured studies** ① West S.L., et al. "A meta-analysis comparing the effectiveness of buprenorphine and methadone." *Journal of Substance Abuse*: 2000 12, p. 405–414 ② Barnett P.G., et al. "A meta-analysis comparing buprenorphine to methadone for treatment of opiate dependence." *Addiction*: 2001, 96, p. 683–690. Copies: for both apply DrugScope.

**Contacts** ① Carolyn Graham, California State University, Fresno, 5300 N. Campus Drive, M/S FF12, Fresno, CA 93740-8019, USA, e-mail cgraham@csufresno.edu ② Paul Barnett, Health Economics Resource Center, VA Palo Alto Health Care System, Menlo Park Division (152), 795 Willow Road, Menlo Park, California 94025, USA, e-mail paul.barnett@med.va.gov.

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