



# Clinical Evidence Handbook

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## Opioid Dependence

K. THYARAPPA PRAVEEN, *2gether Foundation Trust, Gloucester, United Kingdom*

FERGUS LAW, *University of Bristol, Bristol, United Kingdom*

JACINTA O'SHEA, *Avon and Wiltshire NHS Mental Health Partnership, Bristol, United Kingdom*

JAN MELICHAR, *University of Bristol, Bristol, United Kingdom*

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Dependence on opioids is a multifactorial condition involving genetic and psychosocial factors. There are three stages to treating opioid dependence.

- Stabilization is usually by opioid substitution treatments, and aims to ensure that the drug use becomes independent of mental state (such as craving and mood) and circumstances (such as finance and physical location).

- The next stage is to withdraw (detox) from opioids.

- The final stage is relapse prevention.

Methadone and buprenorphine help to stabilize opioid use, as they decrease heroin use and help persons stay in their treatment programs.

- Methadone and buprenorphine seem equally effective at stabilizing opioid use.

Methadone, buprenorphine, and alpha<sub>2</sub>-adrenoceptor agonists (lofexidine, clonidine) can all help persons to recover from illicit opioid dependence.

- Lofexidine and clonidine may be less effective than methadone and buprenorphine in withdrawal, although evidence is weak.

- Ultrarapid withdrawal can help in detoxification, although there are important safety risks in keeping patients heavily sedated, under general anesthesia for a day, or under general anesthesia for a few hours, and outcomes are no better.

Naltrexone can help to prevent relapse of heroin use if combined with psychosocial treatment.

### Definition

Opioids (opiates) are highly addictive, and opioid dependence is a chronic relapsing

disorder. Heroin is the most commonly abused opioid; others include morphine, buprenorphine, codeine, and methadone. Dependence is a cluster of physiological, behavioral, and cognitive phenomena in which the use of a substance takes on a much higher priority for a given individual than other behaviors that once had a greater value.

Diagnosis of dependence syndrome is usually made from a combination of history and examination including urinalysis to corroborate the history, looking for the presence of opioid metabolites (e.g., morphine) in the urine. A definitive diagnosis of dependence should usually be made only if three or more of the following have been present together at some stage during the previous year: (1) a strong desire or compulsion to take opioids; (2) difficulties in controlling substance-taking behavior in terms of its onset, termination, and levels of use; (3) a physiological withdrawal state; (4) evidence of tolerance; (5) progressive neglect of alternative pleasures or interests because of opioid use; and (6) persisting with substance use despite clear evidence of overtly harmful consequences. Physical examination can also provide evidence of acute intoxication, withdrawal, and chronic or physical consequences of drug administration, such as abscesses, malnutrition, poor dentition, and deep venous thrombosis.

When commencing treatment, urinalysis should confirm the use of opioids, and some physicians require that a number of samples be taken several days apart to confirm ongoing use. However, regular urinalysis might not be necessary with continuing treatment because studies report that, in situations in

which there is no coercion, self-reporting of drug use is sufficiently reliable and valid to provide descriptions of drug use, drug-related problems, and the natural history of drug use. However, random sampling is still useful.

All patients in this review were 16 years and older.

**Incidence and Prevalence**

Opioid and intravenous drug use rose substantially in the 1990s. New notifications to the Addicts Index (a register held by the UK Home Office) by physicians of persons dependent on opioids increased more than 30-fold, from approximately 600 in 1966 to more than 18,000 in 1996, and nearly tripled during the 1990s. The UK drug strategy reported 100,000 to 200,000 problem drug users in the mid-1990s. A pilot study of national estimation methods suggested that there were 143,000 to 266,000 problem drug users, with about 75,000 to 150,000 opioid users in England and Wales in 1996. More recently, in 2000, the number of persons becoming dependent on opioids ranged from 13,000 (0.06 per 100 persons 15 to 44 years

of age) to more than 26,000 (0.13 per 100 persons 15 to 44 years of age). A reduction in the supply of heroin in Australia has also cut the prevalence of opioid abuse and dependence in half since the late 1990s. In 2008 and 2009, a report from the National Drug Evidence Centre estimated that there were 262,428 problematic opioid users in England, suggesting a rate of 7.69 per 1,000 persons 15 to 64 years of age.

**Etiology and Risk Factors**

Opioid dependence is a multifactorial condition involving genetic and psychosocial factors. Studies in twins report that both the genetic and shared environmental effects on risk for use and misuse are usually entirely nonspecific in their effects. Environmental experiences unique to the person largely determine whether predisposed individuals will use or misuse opioids.

**Prognosis**

Addictive disorders are chronic relapsing conditions with no known cure. Naturalistic studies have demonstrated that over a five-year period, approximately one-half of individuals recover from the dependence.

EDITOR'S NOTE: Lofexidine is not available in the United States.

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**Clinical Questions**

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**What are the effects of drug treatments for stabilization (maintenance) in persons with opioid dependence?**

Beneficial	Buprenorphine Methadone
Unknown effectiveness	Buprenorphine vs. methadone (both beneficial and seem equally effective)

**What are the effects of drug treatments for withdrawal in persons with opioid dependence?**

Beneficial	Buprenorphine Methadone
Likely to be beneficial	Lofexidine or clonidine
Unknown effectiveness	Ultrarapid withdrawal (antagonist-assisted [naltrexone and naloxone only])

**What are the effects of drug treatments for relapse prevention in persons with opioid dependence?**

Likely to be beneficial	Naltrexone
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