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## **BMJ paper** Management of illicit opioid use

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## Clinical Updates

### **Management of dependent use of illicit opioids**

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### **Box start**

#### **What you need to know**

- Illicit opioid users have complex needs and require agencies to work collaboratively to help them access healthcare, education, employment, and housing
- Illicit opioid users may have multiple health problems associated with premature disability and mortality
- Adopt a consistent, proactive, and non-judgemental approach in all therapeutic contacts with opioid users to counter stigma and pessimism about effective treatment
- Train patients and carers in the first response to opioid overdose, including the use of naloxone treatment kits
- Length of time in treatment with opioid agonists is the strongest predictor of positive bio-psychosocial outcomes and reduces premature mortality

#### **Box end**

Use of illicit opioids, most commonly heroin, has a wide ranging impact on individuals and society.<sup>1</sup> It may lead to dependence, which is best conceptualised using a “chronic disease” model: effective treatments are available, but illness is often characterised by relapses, remissions, and risk of premature death.<sup>2,3</sup>

Across Europe, four trends are noteworthy: a decline in the use of intravenous heroin, a rise in the use of high potency synthetic opioids (for example, fentanyl), a rise in opioid related deaths, and an increase in the number of long term opioid users aged over 40.<sup>4</sup> The widely reported “epidemic” of opioid associated deaths in the US and Canada is also of global concern and has been attributed to under-regulated medical prescribing of high potency synthetic opioids and a growth in internet supply chains.<sup>5-7</sup> Concurrent use of other substances, for example, alcohol, cocaine, benzodiazepines, neuropathic agents, and novel drugs such as “spice,” increases the risk of adverse outcomes of opioid use in all settings.<sup>8-10</sup>

In this review we describe an evidence based collaborative approach to caring for people who are dependent on illicit opioids (heroin or synthetic opioids) and related harms of use and who seek help for their dependence.<sup>11-13</sup>

### **Approach to assessment and management**

The approach we describe consists of four phases: comprehensive assessment, decision making that is shared with the patient, keyworker-led psychosocial interventions, and peer-led support (“mutual aid”), to minimise harm to the individual and community (fig 1). Distilling the current evidence base is challenging, particularly for psychosocial interventions, because of the socio-political and cultural contexts of illicit opioid use and heterogeneity of study design, interventions, and outcomes.

**Fig 1 A four phase approach to assessment and management** [Please supply a caption/title for this figure.]

## Phase 1: assessment

An initial assessment may take place in a specialist drug and alcohol service or in a general practice clinic as an integrated public health commissioned service. The approach is also helpful for a patient seeking help for their opioid use in routine general practice settings and enables a GP to assess dependence, advise on harm minimisation interventions and refer onwards to access treatment including psychosocial interventions. The initial assessment is best conducted as a semi-structured consultation to identify nature and pattern of substance use.

Assess whether the patient meets the criteria for opioid dependence (box 1). Explore their physical and psychosocial needs, and those of carers and children.<sup>16-18</sup> Offer a non-judgmental, supportive attitude towards the patient to build a trustworthy, respectful, and sustainable therapeutic relationship.<sup>19</sup>

Older, long-term users of illicit opioids typically have life-limiting multimorbidity (box 2) and are high users of unscheduled care.<sup>56-58</sup> Co-location of treatment services for blood borne viruses (BBV) can improve the rates of uptake and completion of treatment for the BBV.<sup>59</sup>

### Box start

#### **Box 1 The ICD-10 diagnostic criteria for opioid dependence (adapted from current guidelines)<sup>15</sup>**

Opioid dependence does not develop without a period of regular use, although regular use alone may not induce dependence. A definitive diagnosis of dependence should usually be made only if three or more of the diagnostic criteria have been experienced or exhibited concurrently at some time during the previous 12 months

1. A strong desire or sense of compulsion to take opioids.
2. Difficulties in controlling opioid use behaviours in terms of the onset, termination, or levels of use.
3. A physiological withdrawal state when opioid use has ceased or been reduced, as evidenced by one of the following:
  - a) characteristic withdrawal syndrome (hot/cold sweats, abdominal cramps, etc.)
  - b) use of opioids (or closely related substances) with the intention of relieving or avoiding withdrawal symptoms
  - c) evidence of tolerance, such that increased doses of opioids are required to achieve effects originally produced by lower doses.
4. Progressive neglect of alternative pleasures or interests because of opioid use; increased amounts of time spent obtaining opioids or recovering from their effects
5. Persisting with opioid use despite clear evidence of overtly harmful consequences, such as depressive mood states consequent to periods of heavy substance use, or drug related impairment of cognitive functioning.

## Box end

### History of substance use

- *Tell me why you've come today and what you expect from treatment? [Is this assuming they have come seeking treatment? What if they are in contemplative stage or have not confirmed their substance use?]* Explore motivating factors, treatment goals, support networks (such as the Drug Rehabilitation Requirement mandated by the UK criminal justice system).

- Tell me about the drugs that you currently use and how you prefer to take your drugs? This will help us work out the best care plan together. Ask about recent opioid use, current symptoms of withdrawal or intoxication, and duration of use. Assess the patient's level of opioid dependence and ask about use of other substances and route of administration (intravenous drug use, inhalation, sharing of drug equipment).

- Have you had treatment before for your drug problem? What did or *didn't* work?

- How much are you currently spending and how do you pay for your drugs? This may uncover criminality, abuse, trafficking, or forced sex work.

- Have you any concerns about your sexual health? Do you need contraception? Are you planning pregnancy?

### Medical history

- Are you taking any other medication? Do you have any health problems? Health disorders associated with illicit drug use are summarised in [box 2](#).

- Assess mental health, taking into account the person's current mood and evidence of psychosis or confusion; assess risk of self-harm.

## Box start

### Box 2 Health disorders and social issues associated with dependent illicit opioid use

#### Acute physical disorders

- Overdose and fatality
- Acute blood borne virus infection
- Vascular: acute haemorrhage from arterial access and damage, venous thromboembolism, arterial embolism and aneurysm
- Pulmonary embolus/venous thromboembolism
- Sepsis
- Violent injury/fractures
- Acute asthma

#### Chronic physical, sexual, and reproductive health disorders

- Multiple comorbidities

- Vascular: recurrent venous thromboembolism, chronic venous ulceration, peripheral vascular disease
- Amputation: secondary to arterial/venous insufficiency, infection, lack of self-care
- Skin: chronic pruritus, wound infections, chronic lower limb ulceration
- Gastrointestinal: chronic constipation, nausea
- Chronic blood borne virus infection: hepatitis C, B, HIV/AIDS
- Liver disease: blood borne virus infection associated chronic hepatitis, cirrhosis, hepatocellular carcinoma
- Respiratory disease: early onset chronic obstructive pulmonary disease, uncontrolled asthma, pneumonia, TB<sup>20-22</sup>
- Poor dental health: dental decay, abscesses, extractions
- Sexual and reproductive health: sub-fertility, sexually transmitted infections, low testosterone in men, erectile dysfunction<sup>23 24</sup>
- Poor pregnancy outcomes: unplanned pregnancy, poor nutrition, lack of periconceptual vitamins, late antenatal booking, missed influenza/pertussis vaccination, premature birth, intrauterine growth retardation, fetal addiction syndromes, maternal death

#### **Mental health**

- Depression, anxiety disorder, post-traumatic stress disorder
- Self-injury or suicide
- Severe mental illness: comorbid or substance induced psychoses, personality disorder, delusional disorder, bipolar disorder
- Co-dependence on alcohol and/or other substances

#### **Social issues**

- Poverty: chronic disability and impact on employment and household income
- Interrupted education and skills training
- Domestic violence, family breakdown
- Child safeguarding issues: “looked after” children; safeguarding registration; children’s access to drugs and accidental overdose; observing drug use behaviours
- Adult safeguarding: exploitation, sex work, vulnerable adults, human trafficking
- Criminality: drug related theft, violence, homicide

#### **Box end**

#### **Social history**

• *Where/who do you live with?* Inquire about the person’s accommodation and whether they have a partner or anyone who can support them. Ask whether their partner or other household members use drugs or alcohol, and whether they feel safe.

• *Are there children at home or elsewhere?* Children might be living with a relative or in a statutory care setting (“looked after” or adopted), in which case, ask about contact arrangements. Ask the ages and names of the children and explore the impact of drug use on parenting and social functioning (routines for children

including school attendance, physical or dental health checks), and safe storage of medication. Discuss safeguarding referral according to identified needs <sup>18</sup>

- What jobs, training, and education have you done since school?
- How are you managing for money? Ask about employment, benefits, and debt.
- Are you at risk of harm from anyone? This might include physical, emotional, or sexual abuse by a family member or intimate partner. Consider use of screening tools, such as HARK. <sup>25 26</sup>

### **Routine physical assessment and tests**

Observe the person for evidence of opioid use, which might include intoxication and withdrawal symptoms (for example, hot or cold sweats, abdominal cramps).<sup>27</sup> Examine injecting sites. Undertake urine or saliva tests for opioids and other substances (according to local protocols) to confirm the presence or absence of drugs before initiating opioid agonist treatment. Offer testing for hepatitis A, B, C, and HIV (pre-testing is not a barrier to immunisation for hepatitis A and B). Further physical assessment may be undertaken based on clinical judgement.

### **Phase 2: agreeing a treatment plan**

- The aim of care is to integrate pharmacological and psychosocial treatments to
- build the person's resilience, health, and wellbeing
  - stabilise their environment and
  - reduce the risk of relapse to illicit opioid use.<sup>28</sup>

Identify the person's goals, describe the treatments available, address concerns and expectations, and give them time to consider treatment options. Consider the person's motivation to change. You may wish to apply a transtheoretical model of behaviour change (box 3).<sup>30</sup> The "action" stage in this model,

which includes engagement with a treatment plan (and re-engagement if relapse occurs), is key to effective care, as patient outcomes improve with length of time in treatment.<sup>14</sup>

#### **Box start**

#### **Box 3 Stages of change—the transtheoretical model of behaviour change (adapted)<sup>29</sup>**

1. Precontemplation—has no intention to change behaviour, even when knowing that they have a problem (and thinks others are exaggerating their problem)
2. Contemplation—is more consciously aware of the problem (pros and cons) and develops intentions to change over a period of time



3. Preparation—expresses intention and shows preparation to act, usually over the next month or more
4. Action—Engages in a treatment plan and psychosocial support
5. Maintenance—continues with health behaviour change over the next few years<sup>23</sup>

**Box end**

## **Drug treatment**

There are three usual treatment pathways: opioid agonist treatment, opioid assisted withdrawal treatment, and opioid antagonist maintenance. Opioid agonist treatment is considered first line treatment globally. If taking this approach, the prescriber should ascertain the patient's responses to previous medication, the level of physical dependence, opioid tolerance, and their personal preference.<sup>31-33</sup>

### Opioid agonist treatment

Calculation and titration of opioid agonist treatment dosage is subject to local protocols, with the aim of assisting the person to stop the use of illicit opioids and safely initiate opioid agonist treatment. Using an adequate and responsive replacement dosage regimen substantially improves outcomes, facilitates recovery, and reduces risk of overdose.<sup>34</sup> Conversely, starting at too low a replacement dose reinforces withdrawal challenges and fatalism.<sup>35</sup> Drug treatment services usually monitor supervised opioid agonist treatment and pharmacies dispense the drug.<sup>36</sup> A systematic review reported a substantial reduction in the risk for all cause and overdose mortality in people dependent on opioids who were undergoing opioid agonist treatments.<sup>37</sup> Pooled all-cause mortality rates were 11.3 and 36.1 per 1000 person years in and out of methadone treatment (unadjusted out-to-in ratio 3.20, 95% confidence interval 2.65 to 3.86), and were reduced to 4.3 and 9.5 in buprenorphine treatment (2.20, 1.34 to 3.61).<sup>37</sup> Retention in opioid agonist treatment is the strongest predictor of positive bio-psychosocial outcomes, with buprenorphine treatment being associated with lower mortality rates than methadone treatment.<sup>14</sup>

**Methadone**, a long-acting mu-receptor agonist, usually blocks opioid withdrawal for 24 hours, removing the drive to use drugs. An adequate daily dose increases tolerance, making illicit opioid use less reinforcing. Induction involves careful titration with intensive, frequent monitoring to minimise risk of overdose. Once the dose of oral methadone is stabilised within a therapeutic range, the prescriber maintains or gradually reduces the dosage according to the patient's goal. As methadone has no ceiling effect, it can lead to overdoses when it is used at doses



above a patient's tolerance or when it is combined with other central nervous system depressants (for example, alcohol, benzodiazepines, or other opioids). Perform an electrocardiogram if prescribing >100 mg oral methadone, if the patient's history suggests arrhythmia, or there is a family history of prolonged QT interval.<sup>34</sup>

**Sublingual buprenorphine** is a partial mu-receptor agonist that partially blocks the action of opioid agonists (for example, heroin) and so discourages illicit opioid use. Buprenorphine is titrated to a therapeutic dose and may be prescribed for short or long term opioid agonist treatment. To minimise the risk of diversion to injection use, buprenorphine can be prescribed in a formulation that includes naloxone ("suboxone"), a short acting opioid antagonist that has poor bioavailability when sublingually administered, but blocks buprenorphine effects if injected.<sup>12 35</sup> Buprenorphine has lower lethality than methadone but can still be lethal when combined with other central nervous system depressant substances.<sup>38</sup> Methadone has been available for opioid agonist treatment much longer than buprenorphine or suboxone and has the most comprehensive evidence of efficacy. Flexible dose opioid agonist treatment with methadone leads to greater retention in treatment than does sublingual buprenorphine.<sup>39</sup>

#### Opioid assisted withdrawal treatment

Withdrawal treatment may be offered if the patient's goal is abstinence from opioids. This regimen involves initial opioid agonist treatment and gradual reduction, followed by an out- or inpatient withdrawal programme according to local protocols and tailored to individual circumstances. Lofexidine, an  $\alpha$  2a-adrenergic receptor agonist, may be used to suppress withdrawal symptoms for a patient making a clinically supported, informed decision not to use opioid agonist treatment for withdrawal or with mild dependence.<sup>40</sup>

#### Opioid antagonist maintenance (naltrexone)

Naltrexone is an opioid antagonist that blocks or reverses the action of opioid agonists and so discourages illicit opioid use. Immediate release naltrexone is cost effective but patients report poor adherence compared with the extended release formulation.<sup>41</sup>

### **Phase 3: support for behaviour change**

Psychosocial interventions are widely used to support a change in drug-related behaviours, although uptake and availability varies with treatment setting.<sup>12 42</sup> There

are two categories of intervention intensity: “standard” and “enhanced” care. Both care pathways utilise a multi-agency, multidisciplinary approach.<sup>42</sup>

In standard care, interventions offered by a keyworker include motivational interviewing and brief interventions, relapse prevention, goal setting, problem solving, and recovery planning. Motivational interviewing is an approach to support behaviour change in productive, person centred consultations.<sup>43</sup> “Relapse prevention strategies” aim to help the patient identify, avoid and manage triggers to drug use and build resilience. “Contingency management” is a controversial but effective intervention whereby rewards, such as vouchers, are provided for positive behaviour change.<sup>44-46</sup>

Enhanced care should be offered if there is poor response to standard care or for patients with more complex needs. A residential rehabilitation programme involves living within a therapeutic community over several months and typically includes high intensity cognitive behavioural therapy and 12 step approaches. Psychiatric comorbidities in opioid dependent patients far exceed those in the general population, influence outcomes, and should be treated according to guidelines.<sup>47 48</sup> Patients with dual diagnoses should be offered integrated mental illness and substance abuse treatments, long term follow-up, and tailored psychosocial interventions.<sup>49 50</sup>

### **Harm reduction**

For many patients, change is slow, and continuing IVDU is a challenge [meaning that they continue to use IV drugs?]. The aim is to support change to healthier behaviours, for example, safer use (inhaled use, avoiding solitary intravenous use, correct disposal of drug use equipment) and safer sexual health practices. Education, convenient access to sterile drug paraphernalia, and free condoms can reduce the risk of sepsis, transmission of blood borne virus, and venous thromboembolism. Offer immunisation for hepatitis A and B.<sup>14 51</sup>

### **Emergency care for opioid overdose**

- Offer all patients naloxone “take home” treatment kits and offer carers training in first response and administration.<sup>50-52</sup> Those at highest risk are younger, male, older with physical/mental health comorbidities, users of intravenous drugs, or those recently discharged from prison.<sup>53 54</sup> The “ABCDE” first response is essential, but where an overdose is suspected, administer naloxone (provided in two-dose injection kits) and repeat as necessary while awaiting emergency services. The patient should

be monitored in an urgent care facility for a minimum of four hours.<sup>52 55</sup> Consider other causes of collapse, such as overdose with other drugs, benzodiazepines, alcohol, and medical conditions such as seizure, sepsis, and head trauma.

#### **Phase 4: early recovery**

The key principle of early recovery is to promote stability by addressing health and social needs, recognising that the social determinants and bio-psychosocial outcomes of opioid dependence are interdependent.<sup>11 12</sup> Stability is enhanced by adherence to opioid agonist treatment, regular contact with a keyworker, and addressing other needs, such as healthcare, housing, and safeguarding of children.<sup>12 18</sup> Aftercare programmes include mutual aid groups, education, training, and employment support to enhance self-esteem and self-efficacy. Independent support networks include “SMART” groups and “Narcotics Anonymous,” which offer peer support and build social capital to sustain recovery.<sup>12</sup>

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**Box start****Education into practice**

- How might using the chronic condition model of care for patients who use illicit opioids affect how you consult?
- How might you increase patient, carer, and community level uptake of education and training in the management of overdose, including how to administer naloxone?

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**Box end**

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**Box start****How patients were involved in the creation of this article**

Neil Dolan has lived experience of enhanced care for opioid use and works in drug and alcohol services in primary care.

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**Box end**

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**Box start****Sources and selection criteria**

We reviewed national and international English language clinical management guidelines from the World Health Organization, the UK, the European Union, Canada, and the United States of America. In addition, we used the Cochrane database to identify relevant systematic reviews, undertook a PubMed search for relevant systematic reviews, and hand searched the guideline references for original research relevant to the clinical management approach to illicit opioid use.

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**Box end**

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**Box start****Areas for future research**

Would novel research methodologies (for example use of incentives or experience based co-design) optimise recruitment and address high attrition rates in intervention and cohort studies?

Which interventions improve outcomes of healthcare for physical-mental multimorbidity in the illicit opioid user and where should these interventions be provided?

Are diversified opioid agonist treatment regimens (such as slow or immediate-release oral diacetylmorphine, inhaled opioid agonist treatment, or supervised injected heroin assisted treatment) cost effective and generalisable interventions?

**Box end**

**Box start**

**Online resources for patients who use illicit opioids and/or other substances**

Alcohol and drug misuse prevention and treatment guidance. [www.gov.uk](http://www.gov.uk)

WHO—Treatment of opioid dependence. [www.who.int](http://www.who.int)

Get help with problematic substance use. [www.canada.ca](http://www.canada.ca)

Addiction and dependency. [www.mind.org.uk](http://www.mind.org.uk)

Substance abuse and addiction—the essentials. [www.militaryonesource.mil](http://www.militaryonesource.mil)

Choice of OAT:

<https://www.choiceandmedication.org/sabp/generate/handyfactsheetmethadonevsbuprenorphine.pdf>

**Box end**

**Box start**

**Continuing medical education resources for healthcare professionals**

Principles of drug addiction treatment: a research-based guide (third edition).

[www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/resources](http://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/resources)

American Society of Addiction Medicine—resource links.

[www.asam.org/resources/public-resources/resource-links](http://www.asam.org/resources/public-resources/resource-links)

Opioid dependence. [www.cks.nice.org.uk/opioid-dependence](http://www.cks.nice.org.uk/opioid-dependence)

Standards and guidelines for practices. [www.emcdda.europa.eu/best-practice/standards/treatment](http://www.emcdda.europa.eu/best-practice/standards/treatment)

Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence.

[www.who.int/substance\\_abuse/publications/opioid\\_dependence\\_guidelines.pdf](http://www.who.int/substance_abuse/publications/opioid_dependence_guidelines.pdf)

**Box end**

**Contributorship** I, Caroline Mitchell, the lead author (the manuscript's guarantor) affirm that the manuscript is an honest, accurate, and transparent account of the review being reported; that no important aspects of the review have been omitted; and that any discrepancies from the review as planned (and, if relevant, registered) have been explained.

**Competing interests** The BMJ has judged that there are no disqualifying financial ties to commercial companies. The authors declare the following other interests: none.

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- <eref>15 Guidelines for the Psychosocially Assisted Pharmacological Treatment of Opioid Dependence. Annex 3 ICD-10 codes for conditions covered in these guidelines. <https://www.ncbi.nlm.nih.gov/books/NBK143174/></eref>
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