# Comorbid chronic non-cancer pain and opioid use disorders

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***Patients with chronic non-cancer pain and opioid dependence are difficult to treat effectively. This article reviews the common issues that arise in relation to assessment and treatment, and recommends the adoption of an integrated approach to this patient population.***

Certain clinical populations present heightened challenges to clinicians, either through their resistance to treatment or through treatment-refractory symptoms that produce mutual frustration. Patients with chronic non-cancer pain (hereafter 'chronic pain') and patients who use illicit opioids often fit into this group. Contemporary reviews of these separate groups were analysed to produce a synthesis review of treating this difficult comorbid group. This article identifies the common psychological disorders that coexist with both chronic pain and opioid use disorders.

Assessment and treatment issues are addressed, and an integrated approach is recommended on the basis of this.

## ASSESSMENT

Unilateral stimulus-response models of pain or substance dependence fail to capture the complex interrelationship of involved biopsychosocial variables. Only a comprehensive biopsychosocial assessment procedure will elucidate the full range of treatment needs of patients with comorbid chronic pain and opioid use disorders, and must include a comprehensive pain assessment (*Table 1*), a comprehensive substance use disorder assessment (*Table 2*), and a psychiatric assessment. Validated psychometric tools are available to assist this process (*Table 3*).

### Comorbid chronic pain and opioid use disorders

Up to 60% of chronic pain patients have a current psychological disorder, heightening pain perception and contributing to pain-related disabilities (Dersh et al, 2002). Similarly, over 70% of patients with a drug use disorder have been found to have a current psychological disorder (Myrick and Brady, 2003). Chronic pain and

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**TABLE 1.**
**Pain assessment**

| | |
|---|---|
| Temporal features | Onset, duration, course, pattern |
| Intensity | Average, least, worst, and current pain (use verbal ratings or numeric scores, or visual analogue scales) |
| Location | Focal, multifocal, generalized, referred, superficial, deep |
| Quality | Aching, throbbing, stabbing, burning |
| Exacerbating/ alleviating factors | Posture, activity, weight bearing, or cutaneous stimulation |
| Classification | Nociceptive pain associated with an identifiable noxious stimulus (such as infection or inflammation). An example of chronic nociception is rheumatoid arthritis |
| | Neuropathic pain involves a pathophysiological process arising out of aberrant neuronal plasticity processes |
| | Idiopathic pain occurs in the absence of an identifiable physical or psychological stimulus |
| | Psychogenic pain arises in certain psychiatric disorders |

From Glajchen (2003)

substance use disorders are also associated with one another. Nearly one third of chronic pain patients have been found to have a current substance use disorder, with a lifetime rate up to three times that of the general population (16%) (Dersh et al, 2002). In over 90% of comorbid chronic pain and substance use disorder, chronic pain occurred after the substance use disorder, because substance use disorder behaviour increases the risk of painful illness and accidents (Dersh et al, 2002).

Chronic pain patients are also predisposed to substance use disorder, although some of this association may be the result of non-problematic dependence upon prescribed opioids (Savage, 1996). However, a history of psychopathology does not predict the development of chronic pain, and neither type nor intensity of psychological disorder predicts recovery rates (Dersh et al, 2002).

**Comorbid psychological disorders**

**Anxiety disorder:** Generalized anxiety disorder exists in over 20% of opioid-dependent patients treated with methadone maintenance (Myrick and Brady, 2003). However, the reliable detection of generalized anxiety disorder is impaired in coexistent substance use disorder, as generalized anxiety disorder symptoms are similar to both alcohol and opioid withdrawals (Myrick and Brady, 2003). Lifetime prevalence rates of generalized anxiety disorder in chronic pain patients are no different to those in the general population, although current rates are higher (Dersh et al, 2002). In the vast majority of cases (95%), the anxiety disorder of chronic pain patients preceded their pain. Anxiety plays a large part in maintaining chronic pain behaviours. Fear of activity (and increased pain intensity) can lead to social withdrawal and reduced physical fitness (Dersh et al, 2002).

Social anxiety disorder is primarily associated with alcohol use disorders: while 5% of methadone maintenance patients have been found to have social anxiety disorder, this is less than half that found in the general population (Myrick and Brady, 2003). In contrast, methadone maintenance patients demonstrate a 50% increase in lifetime prevalence of obsessive compulsive disorder over the general population rate, at almost 3% (Myrick and Brady, 2003). Opioid-dependent patients have 10 times the general population prevalence rate for post-traumatic stress disorder (Myrick and Brady, 2003). Opioid withdrawal is also known to exacerbate post-traumatic stress disorder. The lifetime prevalence of panic disorder in methadone maintenance patients is eight times that of the general population (1.5%), with opioid withdrawal hypothesized as one causative factor (Myrick and Brady, 2003).

**TABLE 2.**
**Substance use disorder assessment**

| | | |
|---|---|---|
| Drug history | Reason(s) for presenting for treatment | |
| | Past and current drug use history | |
| | History of intravenous use, and human immunodeficiency virus and hepatitis risk | |
| | Medical history | |
| | Psychiatric history | |
| | Forensic history | |
| | Social history | |
| | Past contact with treatment services | |
| | Drug misuse in partner and/or family | |
| Examination | Motivation ('readiness to change') | |
| | General health | Opioid-related side effects, overdose and withdrawal experiences |
| | | Route specific problems, e.g. smoking and respiratory health, injecting and abscesses or cellulitis |
| | | Needle sharing and blood-borne viruses |
| | | General health, e.g. anaemia |
| | Mental health | General behaviour, e.g. restlessness in opioid withdrawal |
| | | Mood |
| | | Delusions and hallucinations |
| | | Confusional states |
| | Social and family situation | |
| Special investigations | Haematological investigations | |
| | Urine analysis | |
| | Hair analysis | |

From Department of Health (1999)

**TABLE 3.**
**Psychometric assessment tools**

| | |
|---|---|
| Pain | Brief Pain Inventory† |
| | McGill Pain Questionnaire† |
| Substance use disorders | Alcohol Use Identification Test (AUDIT)‡ |
| | Michigan Alcohol Screening Test (MAST) ‡ |
| | Drug Abuse Screening Test (DAST) ‡ |
| | Addiction Severity Index (ASI; McLellan et al, 1992) |
| | Maudsley Addiction Profile (MAP; Marsden et al, 1998) |
| | Drug subsection of the Mini-International Neuropsychiatric Interview (MINI; Sheehan et al, 1998) |
| Comorbid psychological disorders | The Symptom Checklist (SCL-90)‡ |
| | Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders* (American Psychiatric Association, 2000) (SCID)* ‡ |

* cited in Dersh et al (2002); † cited in Glajchen (2003); ‡ cited in Myrick and Brady (2003)

**Mood disorder:** Most research on comorbid affective disorders has focused on major depressive disorder to the exclusion of bipolar disorders. Lifetime prevalence of major depressive disorder in chronic pain patients (54%) is three times that of the general population, with current rates (30–54%) of up to 10 times that of the general population (5%) (Dersh et al, 2002). In opioid dependence lifetime prevalence rates of 16–75% have been found (Myrick and Brady, 2003). However, accurate diagnosis is complicated by the overlap between behavioural symptoms of depression, chronic pain, and substance dependence (e.g. sleep disturbance, motor retardation, loss of energy, change in appetite and weight). Some have considered the possibility that depression and pain are variations on a theme, with Dersh et al (2002) identifying that:

> **'…both nociceptive and affective pathways coincide anatomically. Furthermore, norepinephrine and serotonin, the two neurotransmitters most implicated in the pathophysiology of mood disorders, are also implicated in the gate-control mechanism of pain.'**

At present, depression has usually been found to be a consequence of chronic pain (Dersh et al, 2002). Gatchel's (1991) three-stage model describes the initial (stage one), normal reactions to acute pain of fear, anxiety and worry. Beyond 2–4 months, the pain becomes chronic (stage two), and the patient may experience learned helplessness, distress and anger. In the longer term (stage three), the patient's life can become centred on their pain, with acceptance of the 'sick role'.

***Gatchel's model and biological changes:*** Biologically, the development of chronic pain (stage two) involves neurophysiological plasticity, demonstrable within the dorsal horn of the spinal cord and in the thalamus of the brain, sometimes producing pathophysiological neuropathic pain that persists even after the initial injury has resolved (Basbaum and Jessell, 2000). Interestingly, this neurological plasticity also underlies the brain changes in opioid dependence (Kupfermann et al, 2000), and there are grounds for considering opioid dependence and chronic pain syndromes as developing through generally similar mechanisms (although at different anatomical locations in the brain).

***Gatchel's model and psychological changes:*** Psychologically, this development to stage two involves cognitive mediators. Banks and Kern's (1996) diathesis-stress model describes how these preexisting cognitive styles and/or skills deficits mediate the patient's biopsychosocial responses to prolonged pain. This may explain why personality disorder has been found in half of chronic pain patients: Dersh et al (2002) suggest that this might indicate 'a general deficit in coping skills', as opposed to chronic pain being the consequence of having any specific personality disorder, as 'no specific type of personality disorder was found to predict chronicity'. Indeed, successful pain rehabilitation not only reduces comorbid anxiety and affective disorders, but reduces subsequent diagnoses of personality disorder too. It is possible that subclinical personality disorder traits are the diatheses, which in chronic pain become diagnosable, with pain relief returning them to sub-diagnostic levels (Dersh et al, 2002).

**Personality disorder:** The most common personality disorder associated with opioid use disorders is antisocial personality disorder, with a prevalence rate (24–30%) some 10 times that of the general population prevalence (2.6–3.5%) (Vaglum, 1998). Vaglum (1998) considers whether the characteristic irritability, criminality, recklessness and lack of responsibility seen in antisocial personality disorder is similar to that seen in some opioid-dependent patients, meaning that antisocial personality disorder and opioid dependence may be the same thing in some patients. For others antisocial personality disorder is a predisposing factor, and it is known that conduct disorder in children under 15 years of age predicts both antisocial personality disorder and drug misuse in adulthood (Vaglum, 1998).

Somatoform disorders include pain arising from both medical and psychological causes (although the patient's experience of the pain will be undifferentiated regardless of cause). However, while somatization disorder, conversion disorder and hypochondriasis are uncommon in chronic pain populations (Dersh et al, 2002), pain disorder is likely to be ubiquitous because pain always has a psychological component (Dersh et al, 2002).

## TREATMENT

Treatment of comorbidities can be either parallel, serial or integrated (Watkins et al, 2001). Parallel treatment involved separate services treating their respective disorders concurrently. Serial treatment involves one service treating the primary disorder first, with the second, comorbid disorder being treated only once this

has been successful. Integrated treatment involves the concurrent treatment of all disorders by the same service. It is hypothesized that the latter approach will be most effective in comorbid patients (Watkins et al, 2001). This approach has now been considered for the treatment of chronic pain. The Pain Society (2003) recommend that one practitioner should have overall responsibility for one patient's treatment.

**Pharmacological interventions**

The aim of treatment of opioid-dependent patients is stabilization and/or detoxification, and the prevention of relapse (Department of Health, 1999). It is interesting to consider how well maintenance methadone or buprenorphine may meet the treatment aim in chronic pain, namely the alleviation of pain. However, methadone maintenance patients have been found to report high levels of chronic pain (Jamison et al, 2000), and a quarter attribute their initial drug use as being a response to chronic pain (Rosenblum et al, 2003). There remains the possibility that long-term administration of opioids increases pain sensitivity (e.g. via neuroplastic changes involved in tolerance). Because some patients on long-term opioids report eventual reduction in pain on cessation of opioids, some have concluded that the withdrawal of opioid treatment can be helpful for some chronic pain patients (Savage, 1996).

Those most likely to benefit from opioid treatment are classified by Schofferman (1993) as 'type 2' or 'type 3' chronic pain patients. The former have 'only minimal disability and it appears appropriate for the structural disease', while the latter have 'well defined structural explanation for the pain that is not amenable to specific therapy, either because there is no definitive treatment available or because definitive treatment is contraindicated for medical reasons'. In both cases, psychopathology is absent, and the patient has not usually sought treatment from more than one practitioner at a time.

In contrast, in the more common 'type 1' pain patient:

> **'[the] pain complaint and the level of disability appear far out of proportion to the structural disease and far out of proportion to the pain and disability usually seen in patients with similar structural lesions'.**

Psychopathological comorbidity is common, as is unemployment through disability, and there may be secondary gains in evidence (e.g. compensation payments). Multiple physicians, concurrent benzodiazepine treatment and alcohol-related problems are common. They are most likely to demonstrate behaviours that suggest that opioid treatment is worsening their problems. 'Doctor-shopping', repeated 'lost' prescriptions, multiple unprescribed increases to dosage, worsening pain symptoms, or worsening physical or psychological functioning have all been highlighted as 'warning signs' that prescribed opioids are being abused (Savage, 1996). Prescription forgery, stealing drugs, or buying and selling drugs illicitly strongly suggest serious problems (Savage, 1996). However, such behaviours can also be signs of undertreated pain. Weissman and Haddox (1989) coined the term pseudoaddiction to describe those patients who display such behaviours, but which disappear once adequate analgesia is achieved. Difficulties in accurately distinguishing 'real' addiction from pseudoaddiction have long been recognized to be a problem (Dunbar and Katz, 1996).

However, one empirical test of Schofferman's theory has failed to support his hypothesis that opioid treatment of type 1 chronic pain patients contributes to an iatrogenic 'downhill spiral' (Ciccone et al, 2000). The researchers found that it was benzodiazepine prescription that led to a downward spiral among chronic pain patients.

Alternative analgesics to opioids include antidepressants, anticonvulsants and antiarrhythmics, all of which can be more effective in chronic neuropathic pain than opioids (Chong and Bajwa, 2003). Tricyclic antidepressants (TCAs) are more effective analgesics than the selective serotonin-reuptake inhibitors (SSRIs); however, the latter have fewer side effects and can therefore be better tolerated by patients. Chong and Bajwa (2003) found no grounds on which to recommend one treatment over another; however, psychological comorbidity can inform that choice. TCAs, SSRIs, selective noradrenaline-reuptake inhibitors and anticonvulsants all have antianxiety properties, and are used to treat anxiety disorders. TCAs are more effective than SSRIs in comorbid opioid dependence and major depressive disorder, with SSRIs so far proving ineffective (Myrick and Brady, 2003). Comorbid bipolar disorder and substance misuse disorder is better treated with anticonvulsants than lithium (Myrick and Brady, 2003). Benzodiazepines should be avoided in all cases, although buspirone, a non-benzodiazepine anxiolytic, is an alternative (Myrick and Brady, 2003).

### Non-pharmacological interventions

Techniques drawn from cognitive and behavioural therapies have been adapted for use in chronic pain, substance use disorders, anxiety disorders and affective disorders. Relaxation techniques, coping skills training, cognitive restructuring, exposure and response prevention, and relapse prevention are some of the interventions that have been found to be useful (Dersh et al, 2002; Myrick and Brady, 2003).

## CONCLUSIONS

An integrated approach to the chronic pain patient with comorbid opioid use disorder is recommended. Effective treatment will only be informed by a comprehensive, biopsychosocial assessment process that equally addresses symptoms of pain, substance misuse and psychological disorder. There are a range of effective pharmacological and non-pharmacological interventions that have been successfully applied to each of these areas. **HM**

*Conflict of interest: none.*


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## KEY POINTS

- Chronic non-cancer pain is associated with substance use disorders.
- Substance use disorders are associated with chronic non-cancer pain.
- Chronic non-cancer pain and substance use disorders are both associated with psychological disorders.
- Psychological disorders are associated with both chronic pain and substance use disorders.
- A biopsychosocial assessment is needed to address this complexity.
- Treatment based upon a biopsychosocial assessment will be more effective.
- Integrated provision of assessment and treatment may produce the most effective outcomes.