

Review

Addiction to opioids in chronic pain patients: A literature review

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Abstract

Opioids have proven very useful for treatment of acute pain and cancer pain, and in the developed countries opioids are increasingly used for treatment of chronic non-malignant pain patients as well. This literature review aims at giving an overview of definitions, mechanisms, diagnostic criteria, incidence and prevalence of addiction in opioid treated pain patients, screening tools for assessing opioid addiction in chronic pain patients and recommendations regarding addiction problems in national and international guidelines for opioid treatment in cancer patients and chronic non-malignant pain patients.

The review indicates that the prevalence of addiction varied from 0% up to 50% in chronic non-malignant pain patients, and from 0% to 7.7% in cancer patients depending of the subpopulation studied and the criteria used. The risk of addiction has to be considered when initiating long-term opioid treatment as addiction may result in poor pain control. Several screening tools were identified, but only a few were thoroughly validated with respect to validity and reliability.

Most of the identified guidelines mention addiction as a potential problem. The guidelines in cancer pain management are concerned with the fact that pain may be under treated because of fear of addiction, and the guidelines in management of non-malignant pain patients include warnings of addiction. According to the literature, it seems appropriate and necessary to be aware of the problems associated with addiction during long-term opioid treatment, and specialised treatment facilities for pain management or addiction medicine should be consulted in these cases.

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Keywords: Addiction; Chronic pain; Screening tools; Questionnaires; Incidence; Prevalence

1. Introduction

Opioids have proven useful for the treatment of acute pain (Shang and Gan, 2003; Quigley, 2004; McQuay et al., 2005; Moore and McQuay, 2005) and pain related to cancer (Zech et al., 1995; Portenoy and Lesage, 1999; Carr et al., 2004). During the last 25 years opioids have increasingly been used for the treatment of chronic non-malignant pain as well. In US, the medical use of opioids increased during the nineties, while the abuse of opioids seemed stable during the same period (Joranson et al.,

2000). However, from 1997 and the following five-year period (Gilson et al., 2004) the medical use in US of the four most common opioids used for pain treatment increased markedly: morphine 73%, hydromorphone 96%, fentanyl 226% and oxycodone 403%. In the same period the abuse of opioid analgesics increased from accounting for 5.75% of all drug abuse in 1997 to 9.85% in 2002. Both studies used The Automation of Reports and Consolidation Orders System (ARCOS) as indicator for medical use, and the Drug Abuse Warning Network (DWAN) Emergency Department as indicator of abuse. According to an older source, the majority of abused prescription drugs are obtained through legitimate dispensing (GAO, 1982).

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Denmark has for years had an extremely high usage of opioids mainly prescribed to chronic non-malignant pain conditions (Clausen, 1997; Jarlbæk et al., 2005). New epidemiological data only comprising chronic non-malignant pain patients show that about 3% of the Danish population use opioids regularly (Eriksen et al., 2003). At admission to pain centres 55–71% of the chronic non-malignant pain patients are already taking opioids regularly (Buckley et al., 1986; Aronoff and McAlary, 1992; Becker et al., 1997).

Long-term treatment with opioids may be complicated by development of tolerance, dependency, addiction, abnormal pain sensitivity, cognitive dysfunction, hormonal changes and immune modulation (Savage, 1996; Bendtsen et al., 1999; Sjøgren et al., 2000; Breivik, 2001; Ballantyne and Mao, 2003). Most of the literature on opioid therapy of chronic non-malignant pain patients consist on reports of surveys and uncontrolled case series (Portenoy and Foley, 1986; Bouckoms et al., 1992; Zenz et al., 1992; Pappagallo et al., 1994; Gardner-Nix, 1996; Lorenz et al., 1997; Simpson et al., 1997; Ytterberg et al., 1998; Schofferman, 1999; Quang-Cantagrel et al., 2000; Altier et al., 2001). Recent systematic reviews including controlled studies of chronic opioid therapy (Ballantyne and Mao, 2003; Kalso et al., 2004) showed that the maximal treatment length was 8 months. Obviously, not only study duration, but also designs and small study populations, did not allow for any conclusions concerning addiction problems.

In chronic pain patients, it is well known that opioid treatment may initially be a part of the solution, but later turn into a substantial part of the problem (Eriksen, 2001). Pain cannot be adequately managed when complicated by addictive disease and may even be worsened in this context (Compton, 1994; Mao et al., 1995; Savage, 1996). Therefore, it is mandatory and challenging to identify and manage opioid addiction during therapeutic long-term opioid therapy of chronic pain patients.

This literature review aims at giving an overview of:

- definitions, mechanisms and diagnostic criteria of addiction;
- incidence and prevalence of addiction;
- screening tools for assessing opioid addiction;
- recommended guidelines for opioid use.

2. Definitions, mechanisms and diagnostic criteria

2.1. Physical dependence

Physical dependence is a physiologic adaptation to the continuous presence of certain drugs in the body. Physical dependence is defined as a state of adaptation

that is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist (Savage et al., 2001). Physical dependence is an expected consequence of prolonged use (Portenoy, 1996), but sometimes physical dependence may develop after the use of a dependency-producing drug for only 48 h (Glatt, 1974; Jaffe and Martin, 1980; Morgan, 1985). Physical dependence may occur following the use of drugs producing reward (see later) as opioids and benzodiazepines, but may also occur following the use of drugs with little or no reward potential, such as beta-blockers, alpha-2-adrenergic agents (e.g. clonidine), corticosteroids and tricyclic antidepressants (Savage et al., 2003).

In a classic study, Himmelsbach (1939) measured the consequences of abrupt termination of morphine in habituated patients. The respiratory rate, blood pressure, temperature, basal metabolic rate, blood glucose, blood inorganic phosphate, blood lactic acid and sedimentation rate increased and body weight, caloric intake, and sleep decreased. The manifestations did not return to equilibrium at the same rate: blood levels of glucose, lactic acid, and inorganic phosphate returned to equilibrium within a month and body temperature, caloric intake, sleep and respiratory rate returned to normal values within two to three months.

Other symptoms and signs of opioid withdrawal in opioid treated pain patients include fatigue, yawning, lacrimation, coryza, diarrhoea, piloerection, sweating, mydriasis, irritability, anxiety, abdominal cramping, deep bone pain, muscles aches and increase of their usual pain (Savage, 1996; Mao and Chen, 2003). The maximum intensity of the withdrawal syndrome is observed within two days and the acute withdrawal symptoms usually lasts only 2–3 days. The remaining manifestations return to equilibrium within 4–6 months (Savage, 1996; Jasinsky, 1997).

A low-grade protracted abstinence syndrome characterized by general discomfort, anhedonia, and drug-craving is often seen (Jaffe and Martin, 1980). It has also been postulated that individuals with chronic pain who use frequent doses of short-acting opioids on a regular basis become physically dependent and develop intermittent withdrawal phenomena including arousal, increased muscular tension and receptor “hunger” between doses of medications. These intermittent withdrawal symptoms may act to increase pain (Jaffe and Martin, 1980). In cancer patients and non-malignant pain patients end-of-dose failure, i.e. when pain occurs or is markedly worsened at the end of a dosing interval (Portenoy and Hagen, 1990), has been claimed to be a cause for breakthrough pains (Portenoy and Hagen, 1990; Portenoy et al., 1999; Højsted et al., in press).

The opioid withdrawal syndrome is mediated largely by a noradrenergic mechanism in the locus ceruleus, a different mechanism than the dopaminergic mechanism and limbic sites associated with reward (Melichar et al., 2001).

2.2. Addiction

Physical dependence and tolerance to prescribed drugs do not constitute sufficient evidence of addiction or substance dependence. As mentioned above, they are normal physiologic responses that often occur with the persistent use of certain medications. Addiction or substance dependence unlike tolerance and physical dependence is not a predictable response to exposure for reward-producing drugs but may occur in biologically and psychologically susceptible individuals.

In the literature the terms “addiction” and “dependence” are used by different medical societies and organisations in order to describe the same problem and this may cause confusion among health care providers and patients. In 1964, The World Health Organisation stopped using the term “addiction” and introduced the term “dependence” (World Health Organisation, 2000). The current definition of dependence in general given by the WHO Expert Committee on Drug Dependence (World Health Organisation, 1993) “is a cluster of physiological, behavioural and cognitive phenomena of variable intensity, in which the use of a psychoactive drug (or drugs) takes on a high priority. The necessary descriptive characteristics are preoccupation with a desire to obtain and take the drug and persistent drug-seeking behaviour. Determinants and problematic consequences of drug dependence may be biological, psychological or social, and usually interact”. The core concept of the WHO definition requires the presence of a strong desire or sense of compulsion to take the drug.

In the International Classification of Diseases (ICD-10) (World Health Organisation, 2003), dependence syndrome is described as “a cluster of behavioural, cognitive, and physiological phenomena that develop after repeated substance use and that typically include a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to the drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal state”. The dependence syndrome may be present for a specific substance (e.g. tobacco, alcohol, or diazepam), for a class of substances (e.g. opioid drugs), or for a wider range of pharmacologically different psychoactive substances (e.g. cocaine).

According to the definitions by The American Medical Association (Rinaldi et al., 1988) and the Pain Society in UK (The Pain Society, 2004) addiction to

opioids “is the compulsive use of opioids to the detriment of the user’s physical and/or psychological health and/or social function. Signs of compulsive use include preoccupation with obtaining and taking opioids, apparently impaired control over their use, and reports of craving. Addiction can only be determined by observing these behaviours over time, not on a single event”.

The American Academy of Pain Medicine, American Pain Society and American Society of Addiction Medicine (US) (American Society of Addiction Medicine, 2001) have described opioid addiction as “a primary, chronic, neurobiological disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterised by behaviours that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving”.

Portenoy (1990, 2004) has suggested the following definition of addiction in the context of patients taking opioids for chronic pain: “Addiction is a psychological and behavioural syndrome characterised by evidence of psychological dependence, and evidence of compulsive drug use, and/or evidence of other aberrant drug-related behaviours” (Table 1).

Several attempts to clarify the terminology have been undertaken (Rinaldi et al., 1988; Savage et al., 2003). The Liaison Committee in Pain and Addiction conjointly formed by the American Pain Society, the American Academy of Pain Medicine and the American Society of Addiction Medicine (Savage et al., 2003) have decided to use the term “addiction” for several reasons. One reason is the similarity between the terms physical dependence, substance dependence, and

Table 1

Criteria for diagnosing addiction in the context of patients taking opioids for chronic pain (Portenoy, 1990)

Addiction is a psychological and behavioural syndrome characterised by

1. An intense desire for the drug and overwhelming concern about its continued availability (psychological dependence)
2. *Evidence of compulsive drug use, characterised, for example by*
 - a. Unsanctioned dose escalation
 - b. Continued dosing despite significant side effects
 - c. Use of drugs to treat symptoms not targeted by therapy, or
 - d. Unapproved use during periods of no symptoms
and/or
3. *Evidence of one or more of a group of associated behaviours, including*
 - a. Manipulation of the treating physician or medical system for the purpose of obtaining additional drug (altering prescriptions, for example)
 - b. Acquisition of drugs from other medical sources or from non-medical sources
 - c. Drug hoarding or sales
 - d. Unapproved use of other drugs (particular alcohol or other sedatives/hypnotics during opioid therapy)

drug dependence. Another reason is that the term dependence no longer reflects current understanding of the scientific basis of addiction. [Savage et al. \(2003\)](#) emphasize that three fundamental concepts are important for understanding addiction, and the terminology related to addiction must reflect these concepts: (1) although some drugs produce pleasurable reward, critical determinants of addiction rest also with the user, (2) addiction is a multidimensional disease with neurobiological and psychological dimensions; and (3) addiction is a phenomenon distinct from physical dependence and tolerance.

2.2.1. *Addiction as a neurobiological phenomenon*

Recent studies support the notion that addiction is a brain disease ([Wise, 2000](#); [Lashner, 2001](#)), but genetic, social and environmental factors may contribute to the development of addictive behaviours ([Nedeljkovic, 2002](#)). Current neurophysiologic evidence suggests that the development of addiction is to some extent due to neurochemical stimulation of the brain reward center ([Gardner, 2005](#)). The brain reward system is a specific limbic circuit generating feelings of pleasure. The most important components of the system are the ventral tegmental area in the brain stem, the nucleus accumbens in the basal ganglia and the orbitofrontal cortex. Opioids and other abusable substances produce alterations in brain function, either resulting in euphoria or dysphoria as in withdrawal and a common feature is that they all release dopamine in either the nucleus accumbens, prefrontal cortex, or both. The brain reward circuits include three components ([Gardner, 2005](#)). The first-stage component consists of descending neurons from the frontal cortex synapsing into the ventral tegmental area. The ventral tegmental area contains the cell bodies of the ascending dopamine system. The axons run rostrally through the medial forebrain bundle to limbic and cortical projection areas. These dopamine system neurons constitute the “second-stage” fibres of the reward system. They are the drug-sensitive component of the reward circuitry, which is activated by abusable substances, and the axons terminating in the nucleus accumbens are the most crucial reward-relevant component of the ascending mesotelencephalic dopamine system. “Third-stage” neurons carry the reward signal further to or via the ventral pallidum. The brain reward system is functionally modulated by a wide variety of neurotransmitter-specific neural systems, including GABA, glutamine, serotonin, noradrenalin, enkephaline, endorphin, dynorphine and cholecystokinin. Interconnections between these three stages of reward neurons appear to be importantly involved in regulating the functional set point for hedonic tone, and manipulating the neural interconnections can alter drug-taking behaviour. The reward experience is subject to modification depending on the site of the cascade that is stimu-

lated and on other physiologic effects of the particular drug used. Each reward experience reinforces further use of the drug. Because many drugs share the final end result of reward stimulation, however, other drugs that act on the cascade may be substituted with some approximation of effect. The susceptibility to the development of addiction in some individuals may be due to an alteration in the individual’s limbic or related system that sensitises the individual to the reinforcing effects of a variety of substances.

2.2.2. *Behavioural aspects of addiction*

The definitions mentioned above emphasize that addiction is a psychological and behavioural process that encompasses three types of aberrant drug-related phenomena ([Portenoy, 1996](#)): loss of control over drug use, compulsive drug use, and continued use despite harm. [Portenoy \(2004\)](#) has listed a set of drug-related behaviours that may cause suspicion about addiction in opioid-treated pain patients ([Table 2](#)). Other behaviours have been suggested by [Savage \(1993\)](#) such as frequent late or missed appointments; reporting of many “drug allergies” which limit options for treatment; asking for medications at the end of an appointment; history of no therapeutic response to any treatment except opioids; negatively described interactions with multiple physicians; and disability or pain out of proportion to identified nociceptive process. [Savage \(2002\)](#) has given a short list of patterns that may suggest addiction: “Look for the four C’s” ([Table 3](#)). Any of these behaviours may occur from time to time in patients using opioids appropriately for pain treatment, but a pattern of these behaviours in the context of titrated pain therapy suggests the need for further evaluation.

Another list of useful questions, the answers to which may be helpful in defining whether medications, especially opioids, are being used by the patient in a pathological manner has been set up by [Sees and Clark \(1993\)](#) ([Table 4](#)). Some of these questions may require repeated clinical assessment for proper interpretation (for example, episodes of prescription or medication losses), while others immediately are suggestive of an addiction problem (for example, abuse of illicit drugs).

In a retrospective evaluation of 20 opioid treated patients with chronic pain and addiction problems [Dunbar and Katz \(1996\)](#) assessed the prevalence of six behavioural criteria: unauthorized dose escalation occurring more than once in a 3-month period; frequent telephone calls to the clinic numbering more than two calls per month; “Doctor shopping” or receiving opioids from any other physician or from any emergency room visit; losing or reporting prescription as “stolen”; more than three visits to the clinic without an appointment during a 1-year period; and multiple so-called drug allergies, or intolerance to attempt to change a patients

Table 2

Aberrant drug-related behaviours that raise concern about the potential for addiction in medical patients prescribed opioids for chronic pain (Portenoy, 1990, 2004)

Probably more predictive of addiction

Selling prescription drugs
 Prescription forgery
 Stealing or “borrowing” drugs from others
 Injecting oral formulations
 Obtaining prescription drugs from non-medical sources
 Concurrent abuse of alcohol or illicit drugs
 Multiple dose escalation or other non-compliance with therapy despite warnings
 Multiple episodes of prescription “loss”
 Repeatedly seeking prescription from other clinicians or from emergency rooms without informing prescriber or after warning to desist
 Evidence of deterioration in the ability to function at work, in the family, or socially that appear to be related to the drug use
 Repeated resistance to changes in therapy despite clear evidence of adverse physical or psychological effects from the drug

Probably less predictive of addiction

Aggressive complaining about the need for more drug
 Drug hoarding during periods of reduced symptoms
 Requesting specific drugs
 Openly acquiring similar drugs from other medical sources
 Unsanctioned dose escalation or other non-compliance with therapy on one or two occasions
 Unapproved use of the drug to treat another symptom
 Reporting psychic effects not intended by the clinician
 Resistance to change in therapy associated with “tolerable” adverse effects with expressions of anxiety related to the return of severe symptoms

opioid to another opioid. They found that the criteria correlated well with each other and with a diagnosis of addiction made during the course of therapy by the patient’s pain physician.

2.2.3. Risk factors

Addiction in the context of an addictive disease process is believed to be due to a combination of factors, including genetic predisposition (Enoch and Goldman,

1999), brain reward mechanisms, personal psychological profile, socio-cultural context and drug exposure (Savage, 2002; Lin and Anthenelli, 2005). Apparent risk factors in the context of pain treatment with opioids include a personal or family history of addiction confirmed by several studies. In the study of Dunbar and Katz (1996) the risk factors for non-compliance with the opioid regime in chronic non-malignant pain patients with a history of substance abuse were poly-substance abusers, not being members of the Alcoholics Anonymous or having poor social support. In the study of Compton et al. (1998), patients diagnosed with psychiatric diagnoses of substance use disorders were more likely to show aberrant drug-taking behaviours as unsanctioned dose escalations, receiving opioids from multiple sources and showing loss of control. Michna et al. (2004) found that the presence of two or more risk factors was associated with clinical evidence of opioid misuse. Risk factors included patients or family history of substance abuse or legal problems related to substance abuse. Schieffer et al. (2005) found that patients with history of both drug and alcohol abuse and patients with a prior psychiatric disorder, compared to those without, showed greater medication misuse.

Other variables, such as gender, marital status, age, and psychiatric co-morbidity, may contribute to risk, but the relations are less clear (Savage, 2002).

2.2.4. Diagnostic criteria

The American Psychiatric Association has set up diagnostic criteria for substance dependence (American Psychiatric Association, 1994), the DSM-IV Diagnostic criteria for substance dependence (Table 5). But use of

Table 3

Pattern that may suggest addiction in opioid-treated pain patients (“Looking for the four C’s”) (Savage, 2002)

Adverse Consequences/harm due to use

Intoxicated/somnolent/sedated
 Declining activity
 Irritable/anxious/labile mood
 Increasing sleep disturbances
 Increasing pain complaints
 Increasing relationship dysfunction

Impaired Control over use/Compulsive use

Reports lost or stolen prescriptions or medication
 Frequent early renewal requests
 Urgent calls or unscheduled visits
 Abusing other drugs or alcohol
 Cannot produce medication on request
 Withdrawal noted at clinic visits
 Observers report overuse or sporadic use

Preoccupation with use due to Craving

Frequently missed appointment unless opioid renewal expected
 Does not try nonopioid treatments
 Cannot tolerate most medications
 Requests medication with high reward
 No relief with anything else except opioids

Table 4

Useful Questions for probing addiction in chronic pain patients (Sees and Clark, 1993)

Drug-taking reliability

Does the patient take opioids or other psychoactive medications as prescribed?

Frequency? Dose?

Loss of control or use

Does the patient have partially used bottles of medication at home?

Will the patient bring them in for verification?

Indications of drug-seeking behaviours

Frequently reports losing medication?

Demands drugs of high street value?

Has prescriptions from multiple doctors?

Has prescriptions at multiple pharmacies?

Abuse of drugs other than those prescribed

Alcohol? Cocaine? Marijuana? Heroin? Amphetamines?

Opioids? Benzodiazepines?

Contact with street-drug cultures

Friends or family members who are street-drug users?

Does the patient buy street drugs for any purpose?

Adverse life consequences not due to chronic pain, but due to the effects of opioids or other drugs

Inability to work?

Loss of friends or alienation of family?

Decreased interest in recreational activities?

Adverse health consequences?

Cooperation with full treatment plan and alternative pain management techniques

Avoiding situations that induce pain?

Using non-narcotic medications?

Using physical therapy?

Using TNS units if indicated?

Medication or biofeedback?

These questions should also be asked family members to validate the history from the patients

these diagnostic criteria for dependence in chronic pain patients treated with opioids has been argued by several authors to be inappropriate (Sees and Clark, 1993; Portenoy, 2004; Eriksen, 2001; Savage, 2002). Chronic pain patients in unproblematic opioid treatment may easily fulfil three or more of the criteria: tolerance to opioids are often developed, withdrawal symptoms occur when the patient does not take the opioid, the patient may use the opioid in a larger amount or for a longer period than intended and there may have been unsuccessful efforts to cut down the opioid use because of worsened pain.

According to The International Classification of Diseases (ICD-10) (World Health Organisation, 2003) a definite diagnosis of dependence requires that three or more of the six following characteristic features have been experienced or exhibited: a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to the drug use than to other activities and obliga-

tions, increased tolerance, and sometimes a physical withdrawal state.

In 1990, Portenoy (1990) suggested a set of criteria for diagnosing addiction in the context of patients taking opioids for chronic pain (Table 1).

We consider the Portenoy criteria listed in Table 1 to be the more appropriate for diagnosing addiction in the context of patients taking opioids for chronic pain than the DSM-IV criteria and the ICD-10 criteria.

2.3. Differential diagnoses to dependence and addiction

In certain circumstances drug-seeking behaviour may falsely appear to indicate the presence of addiction. *Therapeutic dependence* (Miotto et al., 1996; Portenoy, 2004) may be present in chronic pain patients receiving adequate relief by opioids who are hoarding opioid analgesics to ensure that he or she continues to receive adequate pain control by “building up” a reserve of opioids (Compton et al., 1998). Such hoarding behaviour may also be found in other groups of patients, such as diabetics, who are dependent on insulin or in patients with angina, who obtain relief from nitro-glycerine. While “insulin-seeking” behaviour by diabetics may seem appropriate, opiate-seeking behaviour by pain patients are likely to be mislabelled as addictive.

Pseudoaddiction is a related phenomenon and results also in “drug-seeking” behaviour (Weissman and Had-dox, 1989). Pseudoaddiction may occur in chronic pain patients, who are prescribed sub analgesic doses of opioids. These behaviours may include drug-seeking behaviour, medication taken in larger amounts than prescribed, running out of medications prematurely, family concerns about the prescriptions, and withdrawal symptoms (Sees and Clark, 1993). These behaviours are not due to addiction, but reflect under-treatment of pain, and consequently adequate pain relief eliminates the abnormal behaviour.

Some patients, especially patients on short-acting opioids, may suffer from recurrent “*subtle withdrawal*”, which is manifested as increased pain (Brodner and Taub, 1978; Jaffe and Martin, 1980; Savage, 1993). It is difficult to differentiate between the primary pain cause and the pain resulting from opioid withdrawal. Patients who increase opioid doses in order to achieve pain relief may actually be treating opioid withdrawal (Brodner and Taub, 1978; Krudow, 1982; Matthews et al., 1990; Fishbain et al., 1992).

Clinical experience suggests that some of the patients may *divert* medications from therapeutic use (Savage, 2002). Patients with pain may share or sell opioid analgesics, and recent reports from different countries indicate that illicit use of prescribed drugs is a major problem (Fountain et al., 2000; Woolf and Hashmi, 2004; Cicero et al., 2005; Haydon et al., 2005). Signs of diversion may include stories that do not seem quite

Table 5
DSM-IV Diagnostic criteria for substance dependence

A maladaptive use, leading to clinically significant impairment or distress, as manifested by three or more of the following, occurring at any time in the same 12-months period

1. Tolerance, as defined by either the following:
 - a. A need for markedly increased amounts of the substance to achieve intoxication or a desired effect
 - b. Markedly diminished effect with continued use of the same amount of the substance
2. Withdrawal, as manifested by either of the following:
 - a. The characteristic withdrawal symptom for the substance
 - b. The same (or closely related) substance is taken to relieve or avoid withdrawal symptoms
3. The substance is often taken in larger amounts over a longer period than was intended
4. There is a persistent desire or unsuccessful efforts to cut down or control substance use
5. A great deal of time is spent in activities despite knowledge of having a persistent physical or psychological problem that is likely to have been caused by or exacerbated by the substance (e.g. current cocaine use despite recognition of cocaine induced depression or continued drinking despite recognition that a ulcer was made worse by alcohol consumption)

The symptoms for substance abuse are

1. Recurrent substance use resulting in failures to fulfil major role obligations at work, school or home
2. Recurrent substance use in physically hazardous situations (e.g. driving or operating a machine when impaired by substance use)
3. Recurrent substance related legal problems Continued substance use despite persistent or recurrent social or interpersonal problems caused by the effects of the substance

right, loss of prescriptions, exaggerating or malingering of symptoms as angina, kidney stones and migraine headaches, and asking for specific drugs (Cole, 2001).

Another differential diagnosis of aberrant drug-seeking behaviour may include cognitive impairment or unrecognised psychiatric disorder (e.g. depression, anxiety, borderline personality disorder) (Passik et al., 2000a), which may preclude the appropriate therapeutic use of opioids (Kirsh, 2002).

3. Incidence and prevalence

Several large studies have been conducted to estimate the general prevalence of drug dependence and addiction in the population. In the National Institute of Mental Health Epidemiologic Catchment Area Program (US) 20,291 persons were interviewed. The estimated US population lifetime prevalence of drug dependence was 6.1% (Regier et al., 1990). The National Comorbidity Survey (US), a structured diagnostic interview, estimated the prevalence of dependence of illegal drugs, non-medical prescriptions of psychotropic drugs and inhalants. They found that 1.8% of the respondents met the criteria for abuse or dependence according to the DSM-III and a lifetime prevalence of 7.5% (Warner et al., 1995). In a study of lifetime prevalence rates of mental disorders in the general population in Germany, Meyer et al. (2000) found – using DSM-IV criteria – a prevalence of drug abuse of 5.2% and drug dependence of 22.6%.

Addiction problems among hospitalised patients in general seem to be rare. The Boston Collaborative Drug Surveillance Project (Porter and Jick, 1980) examined

patients with no history of substance abuse who received at least one dose of an opioid during the hospital stay. Only four cases of addiction among 11,882 hospitalised patients were observed. The criteria used for diagnosing addiction were not reported.

In order to evaluate the prevalence of problems with long-term opioid treatment, a literature search was undertaken for reports of addiction, dependence, aberrant drug taking, abuse, misuse and problematic opioid use among cancer patients and chronic non-malignant pain patients treated with opioids. The review yielded 25 reports in chronic non-malignant pain patients (Maruta et al., 1979; France et al., 1984; Fishbain et al., 1986; Portenoy and Foley, 1986; Zenz et al., 1992; Polatin et al., 1993; Berndt et al., 1993; Gatchel et al., 1994; Pappagallo et al., 1994; Hoffmann et al., 1995; Brown et al., 1996; Moulin et al., 1996; Chabal, 1997; Kouyanou et al., 1997; Ytterberg et al., 1998; Jamison et al., 1998; Schofferman, 1999; Quang-Cantagrel et al., 2000; Dellelijn, 2001; Cowan et al., 2002; Cowan et al., 2003; Adams et al., 2004; Michna et al., 2004; Mahowald et al., 2005; Manchikanti et al., 2005), one study in patients with sickle cell disease (Elander et al., 2003), three studies in patients with migraine and headache (Medina and Diamond, 1977; Langemark and Olesen, 1984; Saper et al., 2004) and five reports in cancer patients (Evans, 1981; Macaluso et al., 1988; Schug et al., 1992; Passik et al., 2000a; Passik et al., 2000b) (Table 6). As can be seen from Table 6 the studies have reported problems with opioid treatment based on behavioural observations, urine toxicology tests, DSM-III and IV criteria, and Portenoy's criteria. None of the studies used ICD-10 criteria. In studies based on behavioural criteria, the prevalences varied from 0% to

Table 6

Incidence and prevalence of addiction problems in chronic non-malignant pain patients and cancer patients treated with opioids

Author and year	Population	Study design	Criteria for abuse, addiction, and substance dependence	Length of opioid treatment Mean (range or SD)	Length of observation period Mean (range)	Number of patients with abuse, addiction, or substance dependence/total sample of patients	Number of patients with abuse, addiction, or substance dependence/total number of patients taking opioids	%
Chronic non-malignant pain patients								
<i>Addiction rate based on behavioural criteria</i>								
Medina and Diamond, 1977	Patients admitted to a headache clinic	Interview Cross sectional	Patients who ingested the medication daily in a dose 50% higher the recommended	0.5–35 years	–		3/24	12.5
Evans, 1981	Chronic pain patients attending a pain clinic	Screening of new patients attending the pain clinic Cross sectional	Subjective evaluation based on drug-seeking behaviour	63% had been taken opioids for more than a year	–		9/56	16.1
France et al., 1984	Chronic non-malignant pain patients at a pain centre	Prospective	Drug-seeking behaviour	13 (6–22) months	13 (6–22) months		0/16	0
Langemark and Olesen, 1984	Patients with migraine admitted to a neurological department	Retrospective medical chart review	Steady increase in dose, dose above recommended, no increase in symptoms after tapering	Not reported	–	32/459		7.0
Portenoy and Foley, 1986	Chronic non-malignant pain patients treated at a pain centre	Retrospective chart review	Unapproved dose escalation and drug diversion	Half of the patients treated for more than 4 years, three patients for more than 10 years	–		2/38	5.3
Zenz et al., 1992	Chronic non-malignant pain patient treated at a pain centre	Prospective	Drug-seeking behaviour	224 (14–1472 days)	224 (14–1472 days)		0/100	0
Pappagallo et al., 1994	Patients with posttherapeutic neuralgia	Prospective (patients with a history of drug abuse excluded)	Drug-seeking behaviour	10 (2–21) months	6 months		0/20	0
Moulin et al., 1996	Chronic pain patients	Prospective (patients with a history of drug abuse excluded)	Drug-seeking behaviour	11 weeks	11 weeks		0/46	0
Jamison et al., 1998	Chronic low back patients	Prospective (patients with a history of drug abuse excluded)	Non-compliance	1 year	1 year		1/36	2.8
Ytterberg et al., 1998	Chronic rheumatic disease pain	Retrospective chart review	Abuse behaviour	133 < 3 months 133 > 3 months	–		4/266	1.5
Schofferman, 1999	Refractory low back pain patients	Prospective (patients with a history of drug abuse excluded)	Addictive behaviour	32 (12–60) months	32 (12–60) months		0/21	0
Quang-Cantagrel et al., 2000	Chronic pain patients referred to a pain clinic	Retrospective chart review	Compulsive drug use	8.8 months (SD 6.3)	8.8 months (SD 6.3)		1/86	1.2

(continued on next page)

Table 6 (continued)

Author and year	Population	Study design	Criteria for abuse, addiction, and substance dependence	Length of opioid treatment Mean (range or SD)	Length of observation period Mean (range)	Number of patients with abuse, addiction, or substance dependence/total sample of patients	Number of patients with abuse, addiction, or substance dependence/total number of patients taking opioids	%
Dellemijn, 2001	Chronic pain patients	Prospective	Addictive behaviour	6 weeks to 2 years	6 weeks to 2 years		0/5	0
Cowan et al., 2002	Chronic pain patients referred to a pain clinic	Prospective	Drug-craving or taking medicine more frequently than prescribed	1.3 years (SD 0.47)	1.3 years (SD 0.47)		0/22	0
Cowan et al., 2003	Chronic pain patients referred to a pain clinic	Retrospective chart review and questionnaire Cross sectional	Uncontrolled and compulsive use; opioid drug craving	14.1 months (SD 1.3)			3/104	2.8
Michna et al., 2004	Chronic pain patients treated at a pain centre	Interviews Questionnaire completed by physicians Chart review Urine toxicology Cross sectional	At least one of six problem drug-related behaviours Urine toxicology: see below	59.5 months (2–360)	–	72/145		49.7
Saper et al., 2004	Patients with headache on daily scheduled opioids	Retrospective Medical chart review	Dose violation, lost prescriptions, multisourcing	At least 3 years	3–8 years		35/70	50
Mahowald et al., 2005	Spine pain patients at a Orthopedic spine clinic	Retrospectively analysis of prescriptions for 3 years Cross sectional	Dose escalation not explained by progression and abuse behaviour (multiple prescribers)	94 patients < 3 months 58 patients > 3 months	–		3/152	5
<i>Addiction rate based on list of behavioural criteria defined by the authors</i>								
Maruta et al., 1979	Chronic pain patients admitted to a pain treatment centre	Interview (history of drug-intake) Cross sectional	Modified WHO, Feighner and DSM-III criteria	Not reported	–	Drug abuser: 59/144 Drug dependent: 35/144		41 24
Chabal, 1997	Chronic pain patients enrolled in a pain clinic	Checklist administered by staff Cross sectional	Prescription Opiate Abuse Criteria	>6 months	–		21/76	27.6
<i>Addiction rate based on urine toxicology</i>								
Berndt et al., 1993	Chronic non-malignant pain patients referred to a pain clinic	Urine toxicology Cross sectional	Detection of opioids in urine not reported by patient	Not reported	–	7/109		6.4

Michna et al., 2004	Chronic pain patients treated at a pain centre	Interviews	(1) Urine toxicology: illicit drug in urine	59.5 months (2–360)	–	(1) 25/145	(2) 17.2
		Questionnaire completed by physicians Chart review Urine toxicology Cross sectional	(2) Urine toxicology: Detection of opioids not prescribed Behavioural criteria: see above			(2) 38/145	(3) 26.2
Manchikanti et al., 2005	Chronic pain patients admitted to a pain centre	Cross sectional	Urine analysis (Rapid Drug Screen) of illicit drugs and non-prescribed opioids	Not reported	–	156/400	39.0
<i>Addiction rate based on DSM-III, DSM-III-R or DSM-IV criteria</i>							
Fishbain et al., 1986	Chronic pain patients treated at a pain centre	Semi-structured psychiatric interview Cross sectional	DSM-III	Not reported	–	30/283	10.6
Polatin et al., 1993	Chronic low back pain admitted to a functional restoration programme	Structured psychiatric interview	DSM-III-R	Not reported	–	Psychoactive substance use: Life time prevalence: 72/200 Current prevalence: 38/200	36
		Cross sectional					19
Gatchel et al., 1994	Chronic low back patients admitted to a functional restoration programme	Structured psychiatric interview	DSM-III-R	Not reported	–	Psychoactive substance use: Life time prevalence: 37/152 Current prevalence: 6/152	24
		Cross sectional					5
Hoffmann et al., 1995	Chronic pain patients referred to hospital	Structured interview (the Swedish version of the Substance Use Disorder Diagnostic Schedule)	DSM-III-R	Not reported	–	Current misuse (analgesics): 8/414 Current dependence (analgesics): 52/414	1.9
		Cross sectional					12.6
Brown et al., 1996	Patients who made three or more visits for back pain to a family practice	Structured interview (The Composite International Diagnostic Interview-Substance Abuse Module)	DSM-III-R	Not reported	–	Analgesic abuse or dependence: Life time prevalence: 11/61 Current prevalence: 5/61	18.0
		Cross sectional					8.2
Kouyanou et al., 1997	Chronic pain patients attending a pain clinic	Structured interview (Psychoactive Substance Use Disorder) and semi-structured checklist	DSM-III-R	Not reported	–	Opioid abuse: 4/125 Opioid dependence: 6/125	3.2
		Cross sectional.					4.8

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Table 6 (continued)

Author and year	Population	Study design	Criteria for abuse, addiction, and substance dependence	Length of opioid treatment Mean (range or SD)	Length of observation period Mean (range)	Number of patients with abuse, addiction, or substance dependence/total sample of patients	Number of patients with abuse, addiction, or substance dependence/total number of patients taking opioids	%
Elander et al., 2003	Sickle cell patients	Semistructured interview Cross sectional	DSM-IV	Not reported	–	(A) Substance abuse: (1) Prescribed analgesic used to control pain: 19/51 (2) Prescribed analgesic use beyond pain control: 0/51 (B) Substance dependence: (1) Prescribed analgesic used to control pain: 16/51 (2) Prescribed analgesic use beyond pain control: 1/51		37 0 31 2
<i>Criteria for addiction rate not reported</i>								
Adams et al., 2004	Chronic pain patients admitted to a pain centre	Questionnaire Cross sectional	Known opioid misusers	Not reported	–		12/111	10.8
<i>Cancer patients</i>								
<i>Addiction rate based on behavioural criteria</i>								
Evans, 1981	Cancer patients attending a pain clinic	New patients attending the clinic were screened Cross sectional	Subjective evaluation based on drug-seeking behaviour	Not reported			0/74	0
Macaluso et al., 1988	(1) Cancer patients, hospitalised (2) New patients in a outpatient clinic	Retrospective review of consultations	Misuse: rapid dose escalation for symptoms other than pain Abuse: stealing prescriptions, seeking drugs from multiple sources	Not reported	12 months	(1) Misuse: 0/468 Abuse: 0/148 (2) Misuse: 4/100 Abuse: 2/100		(1) Misuse: 0 Abuse: 0 (2) Misuse: 4 Abuse: 2
Passik et al., 2000a	Oncology inpatients	Attitude and Behaviour Questionnaire Cross sectional	Aberrant drug-taking behaviour	Not reported	–	4/52		7.7
<i>Addiction rate based on behavioural criteria defined by Portenoy</i>								
Schug et al., 1992	Cancer patients	Prospective	Portenoy's criteria	35.3 days	22,525 treatment days		1/550	0.2
<i>Addiction rate based on urine toxicology</i>								
Passik et al., 2000b	Cancer patients who underwent urine toxicology test during treatment in a cancer center	Retrospectively Cross sectional	Urine screening: Detection of illicit drugs or prescription medication not documented as ordered or given, or alcohol	Not reported	–	95/215		44.2

50% in chronic non-malignant pain patients and from 0% to 7.7% in cancer patients. In non-malignant pain patients studies based on criteria defined by the authors the prevalences varied from 24% to 27.6% and in studies based on urine toxicology from 17.2% to 39%. In one of the cancer studies, Portenoy's criteria were used (Schug et al., 1992); in this study an addiction rate of 0.2% was found. In studies using DSM-III criteria, modified DSM-III criteria, or DSM-IV criteria the prevalences varied from 1.9% to 37%. In a study by Fishbain et al. (1986) the DSM-III diagnosis of current drug dependence includes opioids, barbiturates, sedatives and cannabinoid and may therefore overestimate problems with opioids. In one study, the criteria for addiction was not given (Adams et al., 2004).

Another problem in drawing firm conclusions from these reports is that in some of the studies the prevalences are reported for patients with addiction problems compared with the total sample with or without opioids while in other studies prevalences are reported for patients with addiction problems compared with patients taking opioids.

Nine of the studies were conducted prospectively (France et al., 1984; Zenz et al., 1992; Pappagallo et al., 1994; Moulin et al., 1996; Jamison et al., 1998; Schofferman, 1999; Delleijm, 2001; Cowan et al., 2002; Schug et al., 1992) with a follow-up period from 6 weeks to several years. In four of the studies patients with a history of alcohol, drug and/or substance abuse were excluded (Pappagallo et al., 1994; Moulin et al., 1996; Jamison et al., 1998; Schofferman, 1999). In seven studies, the addiction rates were 0. Only two patients, one chronic non-malignant pain patient (Jamison et al., 1998) and one cancer patient (Schug et al., 1992) were found to have addiction problems in these studies.

Seven studies were conducted retrospectively (Portenoy and Foley, 1986; Ytterberg et al., 1998; Quang-Cantagrel et al., 2000; Cowan et al., 2003; Langemark and Olesen, 1984; Saper et al., 2004; Macaluso et al., 1988). The prevalences were highest in the two studies of patients with headache/migraine, 7.0% and 50%, respectively (Langemark and Olesen, 1984; Saper et al., 2004). In the other studies, the rates varied from 1.2 to 5.3%.

The rest of the studies were cross-sectional studies with rates from 5% to 49.7% in chronic non-malignant pain patients and 0–7.7% in cancer patients. In the study by Passik et al. in cancer patients (Passik et al., 2000b) presenting a prevalence of 44.2% the sample was highly biased, as it was focussed on those patients suspected of substance abuse or aberrant drug-taking behaviour accordingly underwent a urine toxicology screening. The patients were randomly selected from a group of patients who underwent screening during a four-year period.

In conclusion, these results are very difficult to interpret as many studies do not specify what is meant by the terms used for evaluation of addiction as “drug-seeking behaviour”, “addictive behaviour”, “abuse behaviour” etc. The studies using DSM-III and IV criteria may overestimate the prevalences as tolerance and withdrawal symptoms are included as criteria for diagnosing addiction. Furthermore, some of these studies include other drugs and substances than opioids and may therefore overestimate the problems with opioids. As stated above the most appropriate diagnostic criteria for diagnosing addiction in opioid treated chronic pain patients seem to be either the ICD-10 criteria and/or Portenoy's criteria. Unfortunately, no studies in this review used the ICD-10 criteria and only one study Portenoy's criteria.

4. Assessment of addiction and dependence

Validity and reliability of assessment tools for identifying addiction in chronic pain patients are displayed in Table 7. The assessment tools are described in details in Appendix.

The CAGE questionnaire, primarily used for brief screening for alcohol abuse, has been adapted to include drugs (*CAGE-AID*) (Brown and Rounds, 1995). The term CAGE is derived from four keywords: cut, annoyed, guilty, and eye-opener. The questionnaire is administered by patients and consists of four questions with answers of “Yes” or “No”. Positive answers to two or more questions constitute a positive screen. Furthermore, Brown adapted the Short Michigan Alcoholism Screening Test to include drugs too (*SMAST-AID*) (Brown and Rounds, 1995). Positive answers to two or more questions constitute a positive screen. The *CAGE-AID* was validated in 124 patients at a family practice and showed high degrees of sensitivity and specificity whereas the *SMAST-AID* did not.

Chabal (1997) created a five-point *Prescription Opioid Abuse Checklist* based on DSM-III-R parameters to be used by clinicians. The checklist relied on easily observable behaviours in the clinical setting. The checklist was applied to 76 chronic non-malignant pain patients and patients who met three of the five criteria were diagnosed as opioid abusers.

Based on Sees and Clark (1993), Portenoy and Payne (1992), and their own clinical experience Miotto et al. (1996) designed a 42-item questionnaire, *Prescription Drug Use Questionnaire* (PDUQ) to be used in chronic pain patients by trained clinicians. The questionnaire was evaluated by Compton et al. in 52 patients with chronic non-malignant pain (Compton et al., 1998). The patients were classified as belonging to addicted or non-addicted groups based on the criteria developed by the American Society of Addiction Medicine. Patients scoring below 11 did not meet the criteria for

Table 7
Screening tools for addiction problems in chronic pain patients treated with opioids

Questionnaire (author, year)	Validity	Reliability		Construct validity: factorial validity	Criterion validity A. Concurrent B. Predictive	Internal consistency	Test–retest stability
	Content	Construct validity: convergent validity	Construct validity: discriminant validity				
CAGE-AID (Brown and Rounds, 1995)					Sensitivity: 0.70 Specificity: 0.85		
Short Michigan Alcohol Screening Test Adapted to Include Drugs (SMAST-AID) (Brown and Rounds, 1995)					Sensitivity: 0.40 Specificity: 0.95		
Prescription Opiate Abuse checklist (Chabal, 1997)	Expert group		Michigan alcoholism screening test, drug abuse screening test				Inter-rater reliability > 0.9
Prescription Drug Use Questionnaire (PDUQ) (Compton et al., 1998)	Based on literature and own clinical experience	ASAM criteria, modified DSM-IV diagnosis		Varians analysis indicates a highly significant difference among subgroups. Levine's test indicated heterogeneity Scheffe's method indicated that scores of non-addicted subjects differed significantly from both groups of addicted subjects (substance-abusing and substance dependence)	Three items were identified as those being best able to predict the presence of a addictive disease	Cronbach's alpha 0.79 Removal of two factors (disabled, involved in litigation) increased the coefficient to 0.81	
Attitude and Behaviour Questionnaire (Passik et al., 2000)	Clinical experience and specialists in pain and addiction medicine	Aberrant drug behaviour					
Substance Use Questionnaire (Cowan et al., 2001, 2002, 2003)	Based on literature	Withdrawal patterns, General opioid use	Comparison between chronic pain patients and heroin users. Two- tailed test-Fischer's exact test: $P < 0.05$ in all questions				

Screening Tool for Addiction Risk (STAR) (Friedman et al., 2003)	Literature, specialist in pain medicine and addiction medicine	DSM-IV criteria		A close relationship among cigarette smoking, a feeling of smoking too much, and a history of treatment in a drug or alcohol rehabilitation facility	The question: "Have you ever been treated in a drug or alcohol rehabilitation facility" had a positive predictive value of 93%		
Assessment of symptoms of substance dependence and abuse (Elander et al., 2003)	Based on DSM-IV criteria	DSM-IV criteria for: substance dependence				Inter-rater reliability: Kappa coefficient : 0.67–0.88 Pearson correlation: 0.95–0.97	
Screener and Opioid Assessment for Patients with Pain (SOAPP) (Butler et al., 2004)	Concept mapping	Substance abuse Psychological dependence	Self-report: PDUQ Staff report: Aberrant Drug Behaviour Index. +Staff Report + Urine toxicology		SOAPP prediction score: the sum of items with effect sizes (Cohen's D) above 0.40 Sensitivity: 0.91 Specificity: 0.69 Positive predictive value: 0.71 Negative predictive value: 0.90 Positive likelihood: 2.94 Negative likelihood: 0.13	Internal consistency coefficient alpha: 0.74	Pearson product moment correlation between the SOAPP prediction score at baseline and at 6 months follow-up: 0.71
Abuse questions responses (Michna et al., 2004)	Items drawn from addiction literature, reviewed by five specialists in pain and two addiction specialists	Number of problems recalled by the physicians or verified by chart review regarding aberrant drug behaviour Urine toxicology	Discriminant function analysis: 76.6% of the cases were grouped correctly				
Pain Medication Questionnaire (PMQ) (Adams et al., 2004)	Items based on literature addressing opioid misuse and on input from nurses, physicians and psychologists.	CAGE	SF-36 Millon Behavioral Health Inventory	Principal component analyses (Kaiser–Guttman criterion): nine components		Cronbach's alpha: 0.73.	Test–retest reliability: Pearson's <i>r</i> : 19 patients at two points, one-half hours apart: 0.85

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Table 7 (continued)

Questionnaire (author, year)	Validity	Reliability		Construct validity: factorial validity	Criterion validity A. Concurrent B. Predictive	Internal consistency	Test–retest stability
	Content	Construct validity: convergent validity	Construct validity: discriminant validity				
Independent rating of 10 physicians/ psychologists: 9.05 (SD = 0.72) on a 10 point scale	MacAndrew Alcoholism Scale	Correlation coefficients: <0.01	Factor rotation	Physicians ratings of risk for opioid misuse: Pearson's <i>r</i> : 0.36–0.45, <i>p</i> < 0.01, Known status of opioid misuse at entry: <i>p</i> = 0.045	Elimination of item 2, 5, 10, 11, and 13 increased Cronbach's alpha to 0.75		
	Revised addiction potential scale					Two-factor analysis	
	Addiction acknowledgement scale					Factor 1: “Preoccupation with procurement of pain medication”: coefficient alpha: 0.77 .	
	Physician risk assessment for opioid misuse (Inter- rater reliability: 0.74)					Factor 2: “Maladaptive behaviours and side- effects”: coefficient alpha: 0.54.	
Dallas Pain Questionnaire Oswestry Pain Disability Questionnaire Visual Pain Analogue Correlation coefficients: <0.01 Factor analysis yielded two factors (alpha 0.77 and 0.54)							

a substance abuse disorder while all patients with scores above 15 met the defined criteria for a substance abuse disorder.

Responses to three items (patient believes he/she is addicted; increases analgesic dose/frequency; specific drug or route of administration preference) were identified as those most predictable of addictive disease in patients, correctly classifying 92.9% of patients, yielding a goodness-of-fit of 6.0.

Passik et al. (2000a) developed the *Attitude and Behaviour Questionnaire* based on the observations from specialists in pain management and substance abuse. The questionnaire covers issues as medication use, present and past drug abuse, patients' beliefs about the risk of addiction in the context of pain treatment and aberrant drug-taking attitudes and behaviours. The instrument was piloted in 52 cancer patients and 111 women with HIV/AIDS. The study attempted to operationalize the issues of aberrant drug use and examine trends and biases likely to be encountered in future studies. Results were given in percentages. No attempt to validate the questionnaire was made in this preliminary study.

Cowan et al. (2002, 2003, 2001) developed the *Substance Use Questionnaire*. The questionnaire was administered by patients and was evaluated in 168 chronic non-malignant pain patients and 39 street heroin users. The questionnaire was capable of differentiating between chronic pain patients and heroin streets abusers. No summary score or cut-off score was given.

The *Screening Tool for Addiction Risk (STAR)* questionnaire (Friedman et al., 2003) was developed by specialists in pain medicine and addiction medicine and consists of 14 true-or-false questions. The questionnaire was validated in 14 patients with chronic pain and addiction (DSM-IV criteria) and 34 chronic pain patients without addiction. Questions related to addiction were prior treatment in a drug rehabilitation facility, nicotine use, feeling of excessive nicotine use, and treatment in another pain clinic. History of treatment in a drug or alcohol rehabilitation facility was a significant predictor of ongoing addiction with a positive predictive value of 93% and a negative predictive value of 5.9%.

In a study of 51 sickle cell patients, Elander et al. (2003) used a semi-structured interview with 12 symptoms of substance dependence and abuse. Criteria were applied to differentiate between pain-related symptoms, which corresponded to the DSM-IV symptoms but involved analgesics used to control pain, and non-pain related symptoms, which involved symptoms beyond pain management. The interviewer classified each symptom as absent or present, and classified symptoms as pain-related or not-pain related.

The *Screening and Opioid Assessment for Pain Patients (SOAAP)* was designed by Butler et al. (2004) to reflect

the consensus of experts regarding predictive value of aberrant drug related behaviours. The questionnaire was administered to 175 patients with chronic non-cancer pain and re-administered to 95 patients after 6 months. The SOAPP consists of 24 items that could be answered by patients on a five-point Likert-like scale. The SOAAP prediction score sensitivity and specificity was gauged against an index (Aberrant Drug Behaviour Index), and the data suggested that a cut-off score of 7 or higher might be a reasonable choice for a SOAPP cut-off.

Michna et al. (2004) explored the usefulness of questions about an abuse history in predicting problems with prescribing opioids for patients at a hospital-based pain management program. The questionnaire was given to 145 patients with chronic pain who had been or were about to be prescribed opioids. The patients were classified as high risk or low risk on the basis of their responses to questions about past problems with drug or alcohol abuse and history of legal problems. The patients were also asked about history of mental health problems, motor vehicle accidents, smoking behaviour, and whether they were bothered by any adverse effects. The treating physicians completed a questionnaire about problems they had encountered with their patients. Patients were grouped into low risk and high risk groups. Most predictive of subjects within the high-risk group were a positive urine screen, a higher required dose of opioid, and the need for a cigarette within the first hour of the day correctly identified 71.7% of the cases.

Adams et al. (2004) developed the *Pain Medication Questionnaire (PMQ)* in order to assess risk for aberrant behaviours in opioid medication use among 184 chronic pain patients. The questionnaire consists of 26 items reflecting a range of potentially dysfunctional attitudes and aberrant behaviours surrounding the use of pain medicine. Opioid medications are not specifically mentioned in these items, so that patients taking any form of pain medication can be measured on these behaviours and attitudes. Patients respond on a 5-point Likert format scale with each point on the scale given a verbal anchor instead of a number. Subjects falling in the lowest third of scores constituted the low-risk group and subjects falling in the highest third of scores constituted the high-risk group.

5. Guidelines

5.1. Cancer related pain

International guidelines for treatment of pain in cancer patients were published by the World Health Organisation (WHO) in 1986 (World Health Organisation, 1986; Foley and Portenoy, 1993; Stjernsward et al.,

1996) and revised and updated in 1996 (World Health Organisation, 1996b). These guidelines have become the golden standard for the management of patients with pain due to cancer and opioids are the mainstay of therapy. Treatment with opioids is recommended for severe pain not relieved by non-opioids or weak opioids. The guidelines can be summarised in five key points: by the mouth, by the clock, by the ladder, for the individual and attention to detail.

Based on the WHO guidelines, detailed guidelines were published by the Scottish Intercollegiate Guidelines Network in 2000 (Scottish Intercollegiate Guidelines Network, 2000), and in 2001 the European Association for Palliative Care (EAPC) published recommendations concerning the use of morphine and alternative opioids in cancer related pain (Hanks et al., 2001).

In the guidelines oral morphine is recommended as the drug of choice, but other opioids as hydromorphone, oxycodone or methadone as well as other routes of administration should be considered if adequate pain control is not achieved. According to the WHO and the EAPC guidelines, concerns about addiction unfortunately have resulted in widespread under-treatment of cancer patients with pain, although this “opiophobia” is highly overestimated and unfounded (McQuay, 1999). In some countries, the fear of opioid addiction has resulted in laws and regulations that make it unnecessarily difficult to obtain opioids for medical use (World Health Organisation, 1996a).

5.2. Chronic non-malignant pain

For the treatment of chronic non-malignant pain patients with opioids, national and international guidelines have been published in US by Portenoy (1990, 1994, 1996), and by the American Academy of Pain Medicine (AAPM) and American Pain Society (APS) (Haddox et al., 1997), in New Zealand by specialists in pain management and addiction medicine (Schug and Large, 1995), in Australia by the Australian Pain Society (Graziotti and Goucke, 1997), in the Nordic countries and in Europe by pain specialists (Kalso et al., 1999; Kalso et al., 2003), and in Great Britain by the Pain Society (The Pain Society, 2004).

All guidelines point out that the patient should be informed of the risks (including the risk of addiction) and benefits of long-term treatment with opioids. Some guidelines address the problems of poor compliance (Portenoy, 1994; Kalso et al., 2003) and recommend in those cases that treatment should be discontinued (Schug and Large, 1995; Graziotti and Goucke, 1997; Kalso et al., 2003).

A history of alcohol abuse is considered as a relative contraindication by five of the guidelines (Portenoy, 1994; Schug and Large, 1995; Haddox et al., 1997;

Kalso et al., 2003; The Pain Society, 2004) and an absolute contraindication by one (Kalso et al., 1999). Three of the guidelines emphasize the need of special attention in patients with a history of drug or alcohol abuse and recommend that such patients should be referred to a multidisciplinary pain clinic (Graziotti and Goucke, 1997; Kalso et al., 2003) or a specialised drug unit (Portenoy, 2004; The Pain Society, 2004). In Australia, a detailed review by a pain management centre should be undertaken annually (Graziotti and Goucke, 1997).

All but one of the guidelines (The Pain Society, 2004) recommend that opioid therapy should only be considered after all other reasonable attempts have failed (Portenoy, 1994; Schug and Large, 1995; Kalso et al., 1999; American Society of Addiction Medicine, 2001) or have been considered (Haddox et al., 1997; Kalso et al., 2003).

Three guidelines recommend that a second opinion may be sought at a multidisciplinary pain centre before long-term opioid treatment is initiated (Graziotti and Goucke, 1997; Kalso et al., 1999; Kalso et al., 2003). Another guideline recommends that the final decision for initiating opioid treatment should be made by a team of two or more practitioners (Schug and Large, 1995). Most guidelines recommend that a single physician should be responsible for the prescription of opioids (Portenoy, 1994; Schug and Large, 1995; Graziotti and Goucke, 1997; Kalso et al., 1999; Kalso et al., 2003; The Pain Society, 2004).

According to the guidelines, the aims of long-term opioid treatment in chronic non-malignant pain patients are to relieve pain (Kalso et al., 1999; The Pain Society, 2004), to relieve pain and/or improve function (Schug and Large, 1995; Graziotti and Goucke, 1997) or to improve quality of life by relieving pain and improving functional status (Portenoy, 1994; Graziotti and Goucke, 1997; Kalso et al., 2003; The Pain Society, 2004). Another guideline states that attention should be given to the possibility of a decrease in global function or quality of life as a result of opioid use (Haddox et al., 1997).

Sustained-release opioids taken by mouth and by the clock is recommended by all guidelines (Portenoy, 1994; Schug and Large, 1995; Graziotti and Goucke, 1997; Kalso et al., 1999, 2003; The Pain Society, 2004). Two guidelines consider transdermal fentanyl patches a useful alternative for patients with morphine intolerance (Graziotti and Goucke, 1997; The Pain Society, 2004). Four guidelines find that short-acting opioids may be considered for breakthrough pain (Portenoy, 1994; Graziotti and Goucke, 1997; Kalso et al., 2003; The Pain Society, 2004), however, some of the same authors give warnings against the use of short-acting opioids in general (Kalso et al., 1999; Kalso et al., 2003; The Pain Society, 2004). Two

guidelines refuse the use of injections at any time (Graziotti and Goucke, 1997), however, one only allow the use in extraordinary circumstances (The Pain Society, 2004).

Monitoring of treatment is recommended by all guidelines. The monitoring should include pain relief, adverse effects, the patient's functional capacity, quality of life (Graziotti and Goucke, 1997; Haddox et al., 1997; Kalso et al., 1999; Kalso et al., 2003; The Pain Society, 2004) and indications of addiction (Portenoy, 1994; Schug and Large, 1995; Graziotti and Goucke, 1997; Haddox et al., 1997; Kalso et al., 2003; The Pain Society, 2004).

Comparison of guidelines for opioid treatment in cancer patients and non-malignant pain patients reveals both similarities and differences. In both group of patients, an oral opioid treatment with long-acting formulations is recommended as first choice, although evidence is lacking regarding the safety of using long-acting opioids compared to short-acting opioids in long-term treatment (Chou et al., 2003). In cancer patients, breakthrough pain may be treated with short-acting opioids orally or even with injections, which in non-malignant pain patients only may be considered in special cases. Generally, the use of short-acting opioids is not recommended in these patients as fast-acting opioids may have more addictive potential than slow-release formulations due to a more rapid increase of opioid concentrations in the brain (Chou et al., 2003; Knapp et al., 2005).

6. Conclusion

This literature review indicates that the diagnosis of addiction among chronic pain patients treated with opioids is difficult. The common used DSM-III and IV criteria may tend to overestimate the problem. The most appropriate criteria seem to be either the ICD-10 or Portenoy's criteria. Only one of the studies identified for this review used Portenoy's criteria and none of the studies used ICD-criteria. The prevalences found in this review may therefore not be applicable for estimating the extent of problems with addiction in these patients. Prospective studies using appropriate criteria are needed in order to make firm conclusions. With these reservations in mind this review showed that estimates of addiction problems among chronic non-malignant pain patients in long-term opioid treatment varied from 0% up to 50% and from 0% to 7.7% in cancer patients depending of the subpopulation studied and the criteria used.

In cancer patients, the prevalence of addiction is not yet studied as intensively as in chronic non-malignant pain. In chronic non-malignant pain patients the risk of addiction has to be considered and continuously eval-

uated as opioid therapy may be continued for the rest of the patient's life. The problem must also be addressed in cancer patients with longer-lasting pain conditions as addiction may predict and result in poor pain control. If the patient consumes opioids for other reasons than pain control, the result may be worsened pain due to withdrawal and abstinence symptoms. Furthermore, as anti-cancer treatment improves, supportive care becomes long lasting, and the significance of addiction problems may become more marked.

Screening for risk of addiction should be performed before starting a long-term opioid treatment in chronic pain patients, thus providing the physician with clues about the necessity for increased attention in susceptible patients. If opioid treatment results in pain control, better functioning and improved health-related quality of life the treatment should of course be continued, even in patients susceptible for addiction. But the point is that these patients will need special attention with focus on compliance and with an open-minded dialogue about the potential problems and the consequences if the opioid treatment is getting out of control.

The ideal screening tool for addiction in chronic pain patients should be easy for the patient to administer, reliable and well validated and translated into the different languages (Jensen, 2003). Most of the questionnaires identified for this review were not extensively validated. In contrast, the Pain Medicine Questionnaire (Adams et al., 2004) has been thoroughly validated with respect to both validity and reliability. As opioids are not specifically mentioned in the questionnaire, patients may not feel opposed to or prejudiced against the questions. The SOAPP questionnaire (Butler et al., 2004) is also reasonably well validated and should be considered.

Most of the international and national guidelines for opioid treatment of non-malignant pain patients include a warning against addiction. The use of short-acting opioids on demand seems to be a controversial issue in these patients. Ideally, chronic non-malignant pain patients should be screened for risk of addiction using a thoroughly validated screening tool before even considering opioid treatment, and the patients should be carefully monitored during treatment. Any signs of aberrant drug behaviour should be recognised as soon as possible and steps to bring the drug use in control must be taken. Addiction in opioid treated patients should result in referral to specialised treatment facilities of pain management or addiction medicine. In the US and other countries it is illegal for non-certified physicians to manage opioid addiction, once the diagnosis has been definitively made.

Future studies should encompass further development of assessment tools followed by long-term

epidemiological surveys of risk factors for developing addiction in opioid treated chronic pain patients.

Appendix. CAGE questions Adapted to Include Drugs (Brown and Rounds, 1995)

Have you felt you ought to cut down your drinking or drug use?

Have people annoyed you by criticizing your drinking or drug use?

Have you felt bad or guilty about your drinking or drug use?

Have you ever had a drink or used drugs first thing in the morning to steady your nerves or to get rid of a hangover (eye-opener)?

The Short Michigan Alcoholism Screening Test Adapted to Include Drugs (Brown and Rounds, 1995)

1. Do you feel you are a normal drinker or drug user (By normal, we mean you drink or use drugs less than or as much as most other people)
2. Do your wife, husband, a parent, or other near relative ever worry or complain about your drinking or drug use?
3. Do you ever feel guilty about your drinking or drug use?
4. Do friends or relative think you are a normal drinker or drug user?
5. Are you able to stop drinking or using drugs when you want to?
6. Have you ever attended a meeting in the Alcoholics Anonymous, Narcotics Anonymous, or Cocaine Anonymous?
7. Has your drinking or drug use ever created problems between you and your wife, husband, parent, or other near relatives?
8. Have you ever got into trouble at work because of your drinking or use of drug?
9. Have you ever neglected your obligations, your family, or your work for two or more days in a row because you were drinking or using drugs?
10. Have you ever gone to anyone for help about your drinking or drug use?
11. Have you ever been in a hospital because of your drinking or drug use?
12. Have you ever been arrested for drunken driving, driving while intoxicated, or driving under the influence of alcoholic beverages or drugs?
13. Have you ever been arrested, or taken into custody, even for a few hours, because of other behaviour while under the influence of alcohol or drugs?

Prescription Opiate Abuse Checklist (Chabal, 1997)

1. The patient displays an overwhelming focus on opiate issues during pain clinic visits that occupy a significant proportion of the pain clinic visit and impedes progress with other issues regarding the patient's pain. This behaviour must persist beyond the third clinic treatment session.
2. The patient has a pattern of early refills (3 or more) or escalating drug use in the absence of an acute change in his or her medical condition
3. The patient generates multiple telephone calls or visits to the administrative office to request more opiates, early refills, or problems associated with the opiate prescription. A patient may qualify with less visits if he or she creates a disturbance with the office staff
4. There is a pattern of prescription problems for a variety of reasons that may include lost medications, spilled medication or stolen medication
5. The patient has supplemental sources of opiate obtained from multiple providers, emergency rooms, or illegal sources

Prescription Drug Use Questionnaire (Compton et al., 1998)

Evaluation of the pain condition

1. Does the patient have more than one painful condition (i.e., chronic back pain complicated by acute migraine or frequent dental work)?
2. Is the patients disabled by pain (i.e., unable to complete social or vocational activities of daily living)?
3. Is the patient receiving disability (i.e., SSI, workman's comp.)?
4. Is the patient involved in litigation around the pain-precipitating incident?
5. Has the patient explored and/or tried non-opioid or non-pharmacological pain management techniques (i.e., physical therapy, TENS, relaxation, biofeedback) to manage pain?
6. Does the patient believe that his/her pain has been adequately treated over the past 6 months?
7. Does the patient express anger/mistrust of past health care providers?
8. Does the patient believe that he/she is addicted to opioid analgesics?
9. Does the referring physician believe that the patient is addicted to opioid analgesics?

Opioid use patterns

9. a. How long has the patient been on continuous opioids? _____ months

10. Does the patient have more than one prescription provider?
11. Is there a pattern of the patient increasing prescribed analgesic dose or frequency?
12. Is there a pattern of the patient calling in for early prescription refills?
13. Does the patient report using analgesics for symptoms other than those proscribed for (i.e., insomnia, anxiety, depression)?
14. Does the patient save/hoard unused medication or have partially unused bottles of medication at home?
15. Does the patient report supplementing analgesics with alcohol or other psychoactive drugs (i.e., Soma, benzodiazepines)?
15. a. If yes, please list:
16. Have the patient ever forged a prescription?
17. Is there a pattern of the patient reporting losing his/her medication?
18. Does the patient have preferences for specific analgesics and/or routes of medication (i.e., IV, IM routes over oral)?
18. a. If so, please list preferred opioids with routes:
19. Is there a pattern of the patient making emergency room visits for analgesics?
20. Has the patients ever obtained analgesics from no medical (street) sources?
21. Has any M.D./D.D.S. limited care, expressed concern, or refused to prescribe opioid analgesics because of patient's opioid use patterns?

Social/Family Factors

22. Have family members expressed concerns that the patient is addicted?
23. Are family members concerned about opioid analgesics side effects or tolerance?
24. Is there a pattern of family interaction that sustains the patient's opioid analgesic use? (i.e., family member overly concerned re: pain or withdrawal)
25. Is there a pattern of family interaction that sustains the patient's illness behaviour or pain symptoms? (i.e., family member assuming caretaker role)
26. Does the spouse/significant other have a history of alcoholism/drug abuse/drug misuse?
27. Has a family member or friend ever obtained analgesic for the patient?
28. Has the patient ever taken analgesics prescribed for a friend or family member?
29. Does a family member or friend have access (either legal or illegal) to opioid analgesics (i.e., a family member in the medical profession)?

Family History

30. Is there a positive history of addiction (to any drug including alcohol) in the patient's mother, father, sibling or blood relative?
31. Is there a positive history of chronic pain in the patient's mother, father, sibling or blood relative?

Patient History of Substance Abuse

32. Did intoxication play a role in pain-precipitating incident?
33. Has the patient ever been diagnosed with addiction to any drug or alcohol?
34. Does the patient have a drug or alcohol treatment history?
35. Has opioid analgesic detoxification been previously attempted?

Psychiatric History

36. Has the patient ever been diagnosed with a psychiatric disorder?
37. Did psychiatric symptoms precede onset of pain?
38. Is there a large psychological component to the pain condition, other than those related to addiction (i.e., multiple psychological stressors)?
39. Is there evidence of a somatoform disorder?
40. Does the patient report a history of sexual or physical abuse?
41. Does the patient currently meet the DSM-IV criteria for any Axis I, II or III condition?
41. a. If so, please list diagnoses:

Please list all pain-producing medical conditions:

Attitude and Behaviour Questionnaire (Passik et al., 2000)

Subjects responded on 5-point Likert-type scales: Strongly disagree = 0 to strongly agree = 4:

If my physician were willing to prescribe pain medicine in adequate dose, I would consult another physician without telling my physician that I have done this

Cancer pain could be so severe that a person might use non-prescribed drugs to get relief

Having cancer can make a person so lonely that the only way they can feel better is to take a pain or anxiety pill

I would never take a prescription narcotic for pain associated with my cancer that was not prescribed by my physician

Having cancer can make a person so lonely that the only way they can feel better is to take street drugs

Anxiety associated with cancer could be so severe that a person might use alcohol to get relief

If I had anxiety that was not relieved I would not be able to cope with my cancer or its treatment without anxiety drug(?) (word is missing in the text)

If I received a prescription for pain medicine from another doctor I would not tell my doctor about it I would take a medication prescribed for my friend or spouse for the relief of my own symptoms

If my pain or anxiety were severe I would try to get prescription drugs (like morphine or Xanax) from street dealers

Cancer pain could be so severe that a person might use alcohol to get relief

If it were necessary to relieve my pain I would try to get heroin from street drug dealers

I have taken a medication prescribed for my friend or spouse for the relief of my symptoms

It is permissible to use medications prescribed for one symptom to relieve another (i.e. take pain medicine to calm my nerves)

Control of pain and anxiety related to cancer is at least as important as chemotherapy, radiation or surgery

I would never take a prescribed narcotic for the relief of my pain for other reason (such as to relieve anxiety or to help me sleep)

I have lost control of my medicines for pain or anxiety and have taken them in an unacceptable way

Cancer patients should consider taking whatever drugs are necessary for the relief of cancer pain even if their physicians would not approve

Anxiety associated with cancer could be so severe that a person might use illicit drugs (street drugs, like quaaludes) to get relief

I am sometimes afraid that I could lose control over the medications that have been prescribed for pain or anxiety and take them in an unacceptable way

My family is very concerned that I need to take (or may need to take in the future) narcotics for pain relief

Cancer patients should consider taking whatever drugs are necessary for relief of cancer pain even if it prevented them from receiving the best treatment for their cancer

I believe that patients with pain from cancer often become addicted to their pain medications

If my primary doctor refused to give me pain medication because he believed that it would harm me, I would not hesitate to go to another doctor to get pain medication

I worry that my medicine for pain and/or anxiety might make me do something bad

I would never take a medication prescribed for the relief of one symptom and use it to relieve another symptom

The need for pain relief could make people do things that they would never even think of doing

Patients with severe pain should increase their dosage of pain medication to relieve pain without contacting their physician

I believe that the medication I take for the relief of pain, anxiety, or fatigue are harming me in some way

I believe that patients who have nausea and vomiting related to cancer and cancer treatment should be able to smoke marijuana to relieve these symptoms

Having cancer can make a person so angry that the only way they can feel better is to take a pain or anxiety pill

Cancer pain could be so severe that a person might use illicit drugs (street drugs, like heroin) to get relief

Most patients with cancer pain eagerly look forward to their next dose of narcotic analgesic

My medicine for pain and/or anxiety have made me do bad things

Patients should consider the use of cocaine, diet pills, over-the-counter “pep” pills, or “speed” for the treatment of fatigue associated with cancer and cancer treatment

If, from past experience, a patient with cancer knows the dosage of pain medication that is needed to get out of pain, the doctor should give this dosage

If I had pain that was not relieved, I would not be able to cope with my cancer or its treatment without pain medication

Having cancer can make a person so angry that the only way they can feel better is to take street drugs

Patients with pain from cancer often crave their pain medicines

Please circle the percentages of cancer patients you believe: (0, 25, 50, 75, 100%)

Use alcohol or street drugs for symptom control

Increase their dose of pain medicine on their own

Seek out more than one physician for prescription of narcotic analgesics

Get high or euphoric from their pain medicines

Please indicate how frequently you have: (Newer, only rarely, once a month, once a week, daily)

In the past I have drunk alcoholic beverages
 I presently drink alcoholic beverages
 In the past I have used heroin
 I presently use heroin
 In the past I have used cocaine
 I presently use cocaine
 In the past I have used marijuana
 I presently use marijuana
 In the past I have used “downs” (i.e. Quaaludes, barbiturates such as Seconal, Placidyl, Milton, Valium)
 I presently use “downs” (i.e. Quaaludes, barbiturates such as Seconal, Placidyl, Milton, Valium)
 In the past I have used hallucinogens (such as LSD)
 I presently use hallucinogens
 I have purchased narcotics without a prescription
 I have borrowed narcotics from a friend or spouse
 I have taken narcotics from a friend or spouse without informing them
 I have purchased a drug for anxiety without a prescription
 I have borrowed a drug for anxiety without a prescription
 I have taken something for anxiety without a prescription
 I have gone to another physician or to an emergency room to get more medication for pain
 I have gone to another physician or to an emergency room to get more medication for anxiety
 I have gone to another physician or to an emergency room to get more medication for pain and told my doctor later
 I have gone to another physician or to an emergency room to get more medication for pain and never told my doctor
 I have increased my dose of pain medicine and told my doctor later
 I have increased my dose of anxiety medicine and told my doctor later
 I have increased my dose of pain medicine and never told my doctor
 I have increased my dose of anxiety medicine and never told my doctor

I found this questionnaire: interesting, intrusive (nosy), irrelevant, relevant, difficult
 I answered the questions: completely honestly, mostly honestly, not at all honestly
 Questions that I did not answer honestly asked about: drug-taking attitudes, past drug-taking attitudes, present drug-taking attitudes
 I did not answer some questions honestly because: I was afraid it would hurt my treatment, I was afraid my doctor would find out, I was afraid if my doctor knew I had taken drugs, he/she would stop my pain or anxiety medicine, I didn't believe that the doctors

running the study would keep my identity secret, the questions were too personal

Substance Use Questionnaire (SUQ) (Cowan et al., 2001, 2003)

Opioid Withdrawal Questions. This questionnaire is intended to find out how you felt after you have stopped taking your opioid analgesics (painkillers). After not taking your painkillers, within the first 2 days or longer, did you have any of the following symptoms?

Did you have stomach ache? If yes, would you describe it as () mild, () moderate, or () severe.
 Did you feel sick? (after you stopped). If yes, would you describe it as () mild, () moderate, or () severe.
 Were you sick? If yes, would you describe it as () mild, () moderate, or () severe.
 Did you have any diarrhoea? If yes, would you describe it as () mild, () moderate, or () severe.
 Did you have any muscle cramps or aches? If yes, would you describe it as () mild, () moderate, or () severe.
 Did you experience an unusual amount of sweating? If yes, would you describe it as () mild, () moderate, or () severe.
 Did you have a fever? If yes, would you describe it as () mild, () moderate, or () severe.
 Did you experience hot or cold flushes? If yes, would you describe it as () mild, () moderate, or () severe.
 Did you have “gooseflesh” or “goose pimples”? If yes, would you describe it as () mild, () moderate, or () severe.
 Did you have a runny nose? If yes, would you describe it as () mild, () moderate, or () severe.
 Did your eyes water? If yes, would you describe it as () mild, () moderate, or () severe.
 Did you yawn excessively? If yes, would you describe it as () mild, () moderate, or () severe.
 Did you have trouble sleeping? If yes, would you describe it as () mild, () moderate, or () severe.
 Do you think that was due to insomnia or was it because your pain returned?
 Did you notice any change of personality? If yes, would you describe it as () mild, () moderate, or () severe.
 Did you feel anxious? If yes, would you describe it as () mild, () moderate, or () severe.
 Did you feel shaky? If yes, would you describe it as () mild, () moderate, or () severe.
 Did you lose your appetite? If yes, would you describe it as () mild, () moderate, or () severe.
 Did you have any drug craving? If yes, would you describe it as () mild, () moderate, or () severe.

General Opioid Use questionnaire

If you stopped, did you gradually reduce your dose or stop suddenly? Gradually () Suddenly ()

The following questions is to be answered Yes () No ()

Do you have a preference for a certain type of opioid (heroin, methadone, morphine, buprenorphine, etc.)drug?

If yes, what is it? Drug name _____

Do you ever have any craving for opioid drugs?

Do you ever feel you can't stop taking drugs?

Do your family and friends think you are addicted to your drugs?

Do you think you might be addicted to the drugs you take?

Have you ever taken any other drug to increase the effect of opioid drugs?

If yes, what is it? Drug name _____

Do you drink a lot of alcohol?

Have you ever drunk alcohol to increase the effect of your drug?

Do you think you ever lost control over the amount of drugs you take?

Have you ever taken drugs to get high?

Have you ever had any problems due to an overdose of your drugs?

Have you ever encountered any legal problems, such as being arrested for disorderly conduct, due to substance-related intoxication? (drink or drugs)?

Have your ever been in a hazardous or potentially hazardous situation as a result of being intoxicated by your drugs

Have your ever taken drugs by a route other than prescribed, for example by crushing up or injecting a pill?

Do you find you have to take more and more opioids to get the same effect as before?

Have you ever purchased or received prescription-only opioid drugs from somewhere other than a recognised outlet?

Have you ever gone to several different doctors or pharmacies in order to get extra prescription drugs?

Have you lost interest in social or leisure activities as a direct result of taking drugs?

Have you had to give up any social or leisure activities as a direct result of taking drugs?

Do you think that your health suffers because of taking drugs?

Would you still use your drugs even if your health suffered because of them?

Do you feel you have ever neglected anything, either your family, household duties, or your job, because of your drugs?

Do you feel that your personal relationships have suffered as a result of taking your drugs; for example, do

you feel that you have lost friends or fallen out with members of your family?

Have you ever taken or borrowed medicines that were prescribed for a friend or relative?

Do you spend a lot of time thinking about your drugs?

Do you spend a lot of time making sure that you have enough drugs?

Do you have a long history of substance abuse or addiction for which you have had past treatment?

Does anybody in you family have a history of substance abuse or addiction?

Have you ever had to take drugs to stop problems due to drug withdrawal?

Did you have any problems not mentioned?_____

In regard to your painkillers:

After you stopped taking your painkillers, did your physical function improve?

After you stopped taking your painkillers, did your physical function decline?

After you stopped taking your painkillers, did your pain return?

Screening Tool for Addiction Risk (Friedman et al., 2003)

1. Have you felt depressed or anxious over the last 6 months?
2. Have you noticed frequent mood swings over the last 6 months?
3. Are you currently employed?
4. Do you smoke cigarettes?
5. Do you feel that you smoke too much?
6. Do you drink more than three alcohol drinks/day?
7. Have you used recreational drugs during the last year?
8. Have you ever been treated in a drug or alcohol rehabilitation facility?
9. Do you get pain medicine from more than one doctor?
10. Have you been to a pain clinic before?
11. Have you visited an emergency room for pain treatment in the past year?
12. Has anyone in your family (relatives you don't live with) had problems with drug or alcohol abuse?
13. Has anyone in your household (partner, children) had problems with drug or alcohol abuse?
14. Did any family member physically or verbally abuse you when you were a child?

Assessment of pain-related and not-pain related symptoms of drug dependence and abuse (Elander et al., 2003)

Symptom	Initial question	Criteria used to classify positive symptoms	
		Pain-related	Non-pain-related
1. Tolerance	Have you ever found that you were taking more pain medicine to get the same effect?	Tolerance occurred only in association with attempts to control pain	Tolerance associated with attempts to alter mood or occurred when pain was not being experienced
2. Withdrawal	Have you ever found that when you stopped taking pain medication you had unpleasant effects or symptoms or feelings	Withdrawal symptoms occurred only after analgesics had been used to control pain, or when the symptoms consisted of pain returning when analgesics were stopped	Withdrawal symptoms followed use of analgesics in the absence of pain or if analgesics had been used to avoid withdrawal symptoms that did not consist of returning pain
3. Greater use than intended	Have you ever found that you ended up taking more medication than you intended to, or carried in taking it for a longer period than you intended to	Analgesics used in larger doses or for longer only to control pain that was more severe or prolonged than usual	Analgesics used in larger doses or for longer to obtain euphoria, relaxation or changes in mood other than pain relief
4. Attempt to give up or to cut down	Have you ever tried to give up pain medication, or use less?	Attempts focusing on avoiding unnecessary analgesic use or concerns about the effectiveness of analgesics for pain, including side effects	Attempts focused on concerns about dependent aspects of analgesic use unrelated to pain
5. Excessive time spent	Have you ever found you were spending more of your time doing things related to using pain medicine, like getting it, taking it, or getting over the effects of it?	Spending time occurred only in association with attempts to control pain	Spending time associated with attempts to alter mood or occurred in the absence of pain
6. Social impairment	Have you ever found that using pain medication meant that you stopped going to work or being with friends, or that you spent less time on things like that?	Impairments occurred only in association with attempts to control pain	Impairments associated with attempts to alter mood or occurred in the absence of pain
7. Use despite known problems	Have you ever gone on using pain medication even when though you knew it was making something else worse for you	Continued use of analgesics for pain relief despite side effects	Continued use to obtain euphoria, relaxation or changes in the mood, or used despite problems other than physical side effects of analgesics
8. Failing role obligations	Has using pain medication ever meant that you stopped doing things that other people expected you to or needed you to?	Episodes took place only in association with attempts to control pain	Episodes associated with attempts to alter mood or had occurred in the absence of pain

(continued on next page)

Symptom	Initial question	Criteria used to classify positive symptoms	
		Pain-related	Non-pain-related
9. Use in physically hazardous situations	Have you ever used pain medication in situations that could have been dangerous, like when you were driving or using machinery and could have an accident?	Use took place only in association with attempts to control pain	Use associated with attempts to alter mood or occurred in the absence of pain
10. Legal problems	Has using pain medicine ever got you into trouble with the policy or the courts?	Problems arose only from the use of analgesics for the control of pain	Problems involved illicit drugs or arose from analgesics used to alter mood or in the absence of pain.
11. Use despite social or interpersonal problems	Have you ever gone on using pain medication even though it was affecting how you got in with other people?	Problems occurred only in association with attempts to control pain	Problems associated with attempts to alter mood or occurred in the absence of pain
12. Craving	When you are not taking pain medication, have you ever had a strong desire to take some?	Craving involved only desire for pain relief	Craving involved desires for euphoria, relaxation, or changes in mood beyond the relief of pain

The Screener and Opioid Assessment for Patients (Butler et al., 2004)

1. How often do you feel that your pain is “out of control”?
2. How often do you have mood swings
3. How often do you do things that you later regret?
4. How often has your family been supportive and encouraging?
5. How often have others told you that you have a bad temper?
6. Compared with other people, how often have you been in a car accident?
7. How often do you smoke a cigarette within an hour after you wake up?
8. How often have you felt a need for higher dose of medication to treat your pain?
9. How often do you take more medication than you are supposed to?
10. How often have any of your family members, including parents and grandparents, had a problem with alcohol or drugs?
11. How often have any of your close friends had a problem with alcohol or drugs?
12. How often have other suggested that you have a drug or alcohol problem?
13. How often have you attended an AA or NA meeting?

14. How often have you had a problem getting along with the doctors who prescribed your medicines?
15. How often have you taken medication other than the way that it was prescribed?
16. How often have you been seen by a psychiatrist or a mental health counsellor?
17. How often have you been treated for an alcohol or drug problem?
18. How often have your medication been lost or stolen?
19. How often have others expressed concerns over your use of medication?
20. How often have you felt craving for medication?
21. How often has more than one doctor prescribed pain medication for you at the same time?
22. How often have you been asked to give a urine screen for substance abuse?
23. How often have you used illegal drugs (for example, marijuana, cocaine etc.) in the past five years?
24. How often, in your lifetime, have you had legal problems or been arrested?

Abuse Questions (Michna et al., 2004)

1. Is there a history of alcohol or substance abuse in your family, even among your grandparents, aunts, or uncles?

2. Have you ever had a problem with drugs or alcohol or attended Alcoholics Anonymous (AA) or Narcotics Anonymous (NA) meetings?
3. Have you ever had any legal problems or been charged with driving while intoxicated (DWI) or driving under the influence of alcohol (DUI)?

Pain Medication Questionnaire (Adams et al., 2004)

1. I believe I am receiving enough medication to relieve my pain
2. My doctor spends enough time talking to me about my pain during appointments
3. I believe I would feel better with a higher dosage of my pain medication
4. In the past, I have had some difficulty getting the medication I need from my doctor(s)
5. I wouldn't mind quitting my current pain medication and trying a new one, if my doctor recommends it
6. I have a clear preference about the type of pain medication I need
7. Family members seem to think that I may be too dependent on my pain medication
8. It is important to me to try ways of managing my pain in addition to the medication (such as relaxation, biofeedback, physical therapy, TENS unit, etc)
9. At times, I take pain medication when I feel anxious and sad or when I need help sleeping
10. At times, I drink alcohol to help control my pain
11. My pain medication makes it hard for me to think clearly sometimes
12. I find it necessary to go to the emergency room to get treatment for my pain
13. My pain medication makes me nauseated and constipated sometimes
14. At times, I need to borrow pain medication from my friends or family to get relief
15. I get pain medication from more than one doctor in order to have enough medication for my pain
16. At times, I think I may be too dependent on my pain medication
17. To help me out, family members have obtained pain medications for me from their own doctors
18. At times, I need to take pain medication more often than it is prescribed in order to relieve my pain
19. I save any unused pain medication I have in case I need it later
20. I find it helpful to call my doctor or clinic to talk about how my pain medication is working
21. At times, I run out of pain medication early and have to call my doctor for refills

22. I find it useful to take additional medications (such as sedatives) to help my pain medication work better
23. How many painful conditions (injured body parts or illnesses) do you have?
24. How many times in the past year have you asked your doctor to increase your prescribed dosage of pain medication in order to get relief?
25. How many times in the past year have you run out of pain medication early and had to request an early refill?
26. How many times in the past year have you accidentally misplaced your prescription for pain medication and had to ask for another?-

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