



<http://www.diva-portal.org>

This is the published version of a paper published in *Heroin Addiction and Related Clinical Problems*.

Citation for the original published paper (version of record):

Monwell, B., Gerdner, A. (2017)

Opiates versus other opioids – are these relevant as diagnostic categorizations?.

*Heroin Addiction and Related Clinical Problems*, 19(6): 39-48

Access to the published version may require subscription.

N.B. When citing this work, cite the original published paper.

Permanent link to this version:

<http://urn.kb.se/resolve?urn=urn:nbn:se:hj:diva-37848>



Pacini Editore & AU CNS

## Regular article

*Heroin Addict Relat Clin Probl* 2017; 19(6): 39-48

HEROIN ADDICTION &  
RELATED CLINICAL  
PROBLEMS

www.europad.org  
www.wftod.org

# Opiates versus other opioids – are these relevant as diagnostic categorizations?

Bodil Monwell<sup>1,2</sup>, and Arne Gerdner<sup>2</sup>

1-Department of Dependence, Psychiatric Clinic, County Hospital Ryhov, Jönköping, Sweden, EU.

2-Jönköping University, School of Health and Welfare, Jönköping, Sweden, EU.

## Summary

**Background:** For more than three decades, the international diagnostic systems have used the term ‘opioids’, including opiates, yet research publications continue to use an older terminology. In 2010, new Codes of Statutes for “opiate replacement therapy” (ORT) was brought into effect in Sweden, stating that only those “dependent on opiates” – explicitly described as heroin, morphine or opium – were eligible. Those addicted to other opioids were then denied access. This study examines the relevance of the distinction of opiates vs. other opioids. Are there differences in the severity of opioid dependence or concerning other substance-related diagnoses? **Methods:** Ninety-nine individuals participated: 1) *the opiate group* (n = 69), and 2) *the other opioids group* (n=30). Structured interviews covered the ICD-10 criteria of nine different types of addictive substances. For opioids, questions were asked separately in relation to opiates versus other opioids. **Results:** The two groups fulfilled the criteria for opioid dependence to the same extent, with most participants meeting all six criteria, so indicating a severe opioid dependence problem. Both opiates and other opioids had contributed to their development of opioid dependence, and both groups, to the same high degree, showed comorbidity affecting other dependence conditions. **Conclusions:** This study reveals that the two categories of opioids used contribute to the development of opioid dependence and that the term ‘opioids’ can be suitably used to convey a unitary concept in diagnostic terms. There was no support for treating the two groups differently. The study calls for more stringent use of terminology in accordance with the international diagnostic systems.

**Key Words:** Maintenance treatment; Buprenorphine; opioid; opiate; dependence; diagnosis; nosology

## 1. Introduction

Probably for as long as eight millennia opiates have been used for their euphoric and pain-relieving effects [31], starting with opium and later followed by its derivatives, *e.g.* morphine and heroin [5]. The problems that arise from such use have likewise long been known, *e.g.* overdoses and a high risk of developing a serious dependence condition, with symptoms such as craving, tolerance, and withdrawal problems [4, 30, 45]. Other opioids were developed with similar effects, some of which, *e.g.* methadone and buprenorphine, were introduced for replacement treatment in the case of severe opioid dependence problems [17, 49]. Other opioids, however, can also be used for getting high, and they too may lead to dependence problems, regardless of whether the sub-

stance is a prescribed medication or bought on the illegal market [15, 25, 50].

The consumption of other opioids has increased like an avalanche worldwide [15, 18, 29, 32, 41, 50, 51]. In 2014, the UN estimated the prevalence of opioid use, including opiates, *i.e.* substances produced from the opium poppy – opium alkaloids – particularly heroin, in the 15-64 age group, to be 33 million individuals [50]. Of these, 17.4 million were estimated to primarily use opiates. There is a plethora of substances within the main group of opioids, and new ones are being introduced continuously [15]. In the USA, the misuse of “prescription opioids”, *e.g.* oxycodone and fentanyl, increased dramatically in the last few decades [7-9, 22]. In Finland, buprenorphine is the main opioid for which opioid dependence treatment is applied, and in Estonia, fentanyl is the

most common opioid which leads to Opioid Replacement Therapy (ORT) [15, 50]. The UN – in the World Drug Report, 2016 – stated that: “opioids remain major drugs of potential harm and health consequences” [50, p. X.].

There is some confusion concerning the concepts of *opioids* and *opiates*. Opioids are the name of the substance group that induces a state of dependence (F11.2 in the ICD-10 [53] and 304.00 in the DSM-IV [1]) according to both international diagnostic systems, regardless of which opioid substance is used. From a biological perspective, all opioids activate the opioid receptors in the brain [4, 45, 49], while *opiates*, *i.e.* opium alkaloids, constitute a subgroup *within* opioids according to the ATC classification (Anatomical Therapeutic Chemical classification system) [54]. Consequently, the previous diagnostic terminology *opiate dependence* was changed to the broader terminology *opioid dependence* in DSM-III in 1980, and, since 1997, ICD-10 has adopted the same terminology. Later versions of the DSM (DSM-IV and DSM-5) continue to refer to opioids as the general term, although DSM-5 [2] changed the word “dependence” to “substance use disorder”. For two decades now, neither of the two global diagnostic systems have referred to “opiate dependence”, and yet that term is still common in research. A recent search in Google Scholar on “opiate dependence” produced 17,500 hits from the last four years, and the correct term “opioid dependence” 18,900 hits. Even when we restrict our search to PubMed to concentrate on the papers of medical journals that should be more aware of the proper diagnostic terminology, we find about the same ratio between frequency of usage of the two terms: 4,159 hits for the last four years on “opiate dependence” and 4,966 hits on the more proper “opioid dependence”.

ORT is an evidence-based treatment of opioid dependence that offers pharmacological treatment with methadone or buprenorphine, combined with offering psychosocial treatment and support interventions [46, 55]. In 2016, ORT was available in 80 countries [25]. The *Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence* [50] address the premises of ORT and recommend that it be based on the ICD-10 or DSM-IV diagnoses, *i.e.* without differentiating between opiates and other opioids. There is a large body of research on ORT, summarized in a systematic review by Connock *et al.* in 2007 [11]. The studies included in the review reflect the above-mentioned terminological confusion on opioids/opiates. The review, however, contained

studies on ORT provided to users of heroin and other opiates as well as to users of various other opioids, and concluded that treatment with methadone or buprenorphine for opioid dependence is cost-effective, thus providing support for the WHO guidelines.

Sweden is traditionally a restrictive country when it comes to drug policy. Although ORT was introduced in Sweden in 1966 (the first country outside the USA) it has always been fenced by restrictions [24, 28]. The imposed rules concerning eligibility in the regulatory documents from the Swedish Board of Health and Welfare (NBHW) were originally strict, but gradually shifted until ORT became the recommended treatment for “opiate dependence” in 2004. The term “opiate dependence” may have been used by the NBHW due to a mistake, since the term opioid was mistranslated into the term opiate in the Swedish versions of the DSM-III, DSM-IV and ICD-10 [26].

Based on reviews by Connock *et al.* [11] and Mattick *et al.* [34], the Swedish Agency for Health Technology Assessment (SBU) published a commentary report that concluded that treatment of opioid dependence with buprenorphine as well as methadone were cost-effective, making no differentiation between type of misused substance, *i.e.* opiates *vs.* other opioids [47].

In March 2010, a new and more restrictive regulation concerning all other opioids was introduced in Sweden. New Codes of Statutes, authored by the NBHW, stated that only applicants with documentation proving they were “dependent on opiates” – here explicitly defined as heroin, morphine or opium – could be accepted for ORT [38]. The imposed regulation did not regard opioid dependence as a criterion for eligibility. From that date, ORT programmes were only allowed to accept those with misuse of heroin, opium, or morphine, which had to be explicitly mentioned in acquired documents (*e.g.* from emergency departments concerning overdoses, or from the police concerning illegal possession) for at least the previous 12 months, and to deny those with similar documented misuse of other opioids (*e.g.* ketobemidone or fentanyl), regardless of health condition and hazardous situation. It was mentioned in the statutes that there was a lack of evidence about the effectiveness of ORT for anyone other than those “dependent on opiates” – thus ignoring the SBU commentary report. Concerning patients who had primarily misused opioids other than heroin, morphine or opium, the NBHW (2009-08-14) instead argued that “these people addicted to pills should not be treated with the same substance” and that they “can be treated with

drugs without dependence potential”, as if the latter had a less severe dependence problem [39]. No reference in support of that statement was provided.

The exclusion of persons dependent on opioids other than heroin, morphine and opium gave us reason to initiate a research project on those applying for ORT, including those who had misused other opioids. A central topic of this project was whether the two groups defined according to the Swedish Code of Statutes of 2010 differed in needs and problem severity.

There are several previous studies comparing different subgroups of misused opioids. Previous research uses various categorizations, *e.g.* heroin, opiates, opioid-analgesics, prescription opioids, non-prescription opioids, oxycodone, to define subgroups, but these terms are given different meanings in different publications and in different countries [7, 11, 13, 44, 56]. In any case, no other study has been found defining the two groups as categorized in the Swedish Code of Statutes of 2010.

A previous study by this team investigated differences between these groups pertinent to needs for clinical and other services based on interviews using the Addiction Severity Index [35]. It concluded that there were great similarities in problem severity between the two groups. Members of the ‘opiate group’ more often had Hepatitis C and more often had to contend with legal problems related to financing their substance misuse. In both groups the great majority, 90 and 75 per cent respectively, mostly injected the drugs, and nearly all those included in the two groups, 96 and 91 per cent respectively, had misused most of the other types of drugs. Both groups, to a similar degree, had severe problems in all the other related areas investigated – physical and psychiatric health, economic provision, legal status, social relations and alcohol problems. Problem severity may, however, be interpreted differently, from a diagnostic perspective, *i.e.* the degree to which the two groups meet diagnostic criteria.

Several questions then arise: Are there differences between the groups in how they meet the criteria of opioid dependence as defined in ICD-10? Do the two groups differ in the extent to which they also meet other substance dependence diagnoses? A broader question – not directly related to the group categorization used in the Swedish Code of Statutes – is whether there is support for a need to continue using “opiate dependence” as a specific diagnostic entity, so separating it from the more general “opioid dependence”? Are there differences in how the misuse

of opiates *vs.* other opioids by patients seeking ORT results in fulfilling the criteria for opioid dependence? These questions are motivated by the continued use of such terminology in the rich international body of research.

The aim of the present paper is therefore to study the diagnostic outcomes concerning substance use diagnoses according to ICD-10, using a validated structured instrument, and comparing two groups of patients seeking ORT, *i.e.* those who have problems with opiates as documented by police or emergency departments for more than 12 months, *vs.* those with similar documented problems with other opioids. More specifically, the following questions will be addressed:

1. Do the two groups meet the criteria for opioid dependence to the same extent?
2. Is there a difference in severity of opioid dependence (number of criteria met)?
3. Do opiates and other opioids contribute in different ways to diagnoses of opioid dependence?
4. What other substance dependence diagnoses do the two groups meet, and do the number of substance dependence diagnoses differ between the two groups?

## 2. Methods

In this study, the catchment area for ORT treatment was Jönköping County in southern Sweden, with a total population of 340,000 inhabitants. This is a sub-study within a longitudinal study of persons assessed for ORT during 2005–2011. A total of 99 individuals (19 women, 80 men) participated in this sub-study. Their mean ages were 35.2 (sd=9.9) for women and 38.5 (sd=11.4) for men. They had all used drugs for more than 20 years. Eighty-seven per cent injected drugs and had done so for more than 13 years. In other words, this was a group with extensive and serious problems. Twenty-nine per cent had migrated from geographical areas in which heroin or opium were the main opioids misused. Jönköping County, however, had traditionally not been such an area, and the misuse of other opioids had been predominant (police information).

The population was divided into two groups, based on the terminology of the Code of Statutes of 2010, and labelled: 1) the *opiate group* – those found in documentation such as medical or police records to have a confirmed addiction, lasting at least 12 months, to “opiates” (n = 69), and 2) the *other opioids*

group (n=30) – those found in similar documentation to have a confirmed addiction to other opioids. Thus, the categorization was made prior to the structured diagnostic interview that was part of this study.

The diagnostic interview was based on ADDIS (Alcohol and Drug Diagnostic Instrument) [52], which is a Swedish translation of the American instrument Substance Use Disorder Diagnostic Schedule (SUDDS) [12]. ADDIS is a structured instrument designed to collect information through the diagnostic assessment of alcohol and drug problems by trained and certified interviewers, and it provides the tools to supply this information in a structured format for formulating diagnoses according to the system that is preferred, *i.e.* ICD-10, DSM-IV or (in a coming version) DSM-5. ADDIS showed substantial to perfect sensitivity and specificity when compared with a LEAD golden standard (Longitudinal, Expert, All Data) for alcohol and drugs [21], while global consistency (test-retest reliability) showed almost perfect systematic correlations on the criteria level in identifying specified drug categories as well as excellent overall internal consistency [20].

ADDIS consists of 75 basic questions posed to patients/clients, of which 47 symptom questions are directed to the person's use, experience and perceived consequences of alcohol and drugs. These 47 questions are asked in relation to each of the following substance groups if used by the interviewee: alcohol, sedatives, analgesics, cannabinoids, amphetamines, cocaine, opiates, hallucinogens, inhalants and mixed polydrug use. The instrument comes with two diagnostic checklists for assessing dependence and harmful use according to ICD-10. The time required for its implementation was scheduled to be 90 minutes, but the interviews actually took between 1 and 3 hours for the population examined in this study, due to the number of substances they had used.

ADDIS includes a substance list of suggested substances in various types of drug groups. This list proved to be inadequate for this research project because it did not include all relevant substances, and was not based on the categorization of opioids in line with the ATC (Anatomic Therapeutic Chemical) classification system [54]. Within the framework of the research project, it was therefore necessary to develop a substance list based on the categorization: opiates *vs.* other opioids, following the substance classes defined in the ATC registry, *i.e.* with opium alkaloids defined as opiates. Different kinds of drugs within the opiate group were specified, *e.g.* heroin, morphine, opium, Dolcontin, and Oxycodone; in the same way,

all other opioids were specified too, *e.g.* Tramadol and fentanyl. The development of the drug list – along with its function, validity, and the distribution of specific substances – has been described in detail by Monwell *et al.* [36].

ADDIS provides specific diagnoses according to both ICD and DSM for specific substance categories under each scheme, in terms of both lifetime and of the previous 12 months [20]. The interviews were carried out to investigate the situation prior to ORT assessment. Since this is a retrospective approach, with the possibility of errors in recollection, the interviews were corroborated by checking against all available documentation from the inquiry conducted for ORT assessment, finding no grounds for questioning the validity of the interviews. The ORT assessment – using previous documents instead of structured diagnostic interviews with the limited purpose of confirming an opiate addiction according to the statutes – was too narrow in its scope to allow detailed diagnostic evaluation. The data could, however, be compared later with data from the more detailed ADDIS interview. All the ORT assessment data pertinent to dependence criteria arising from the misuse of opiates and other opioids, respectively, were confirmed in the ADDIS.

In this study, the main focus has been on lifetime diagnoses based on ADDIS, and the main comparison has looked for possible distinctions between the opiates group and the other opioids group, as categorized by drawing on the documentation collected for the ORT assessment.

Statistical analysis was done in SPSS. The significance of differences was tested using the Chi-squared test for categorical variables (diagnoses) and the Mann-Whitney U-test for the number of additional substance use diagnoses, the latter being a skewed distribution from 0-8. The conventional significance level of  $p < 0.05$  was applied.

The study has been subjected to ethical review and was approved by the Regional Ethical Review Board in Linköping, 2011-06-15 (2011/214-31). The interviewees consented to participating after being informed that the objective of the study was to assess substance use disorder diagnoses for research, and that the findings would not affect their participation in ORT in any way, neither positively, nor negatively.

### 3. Results

First, in Table 1, the two groups – called the *opiate group* and the *other opioids group* – are compared on the issue of whether the criteria for opioid depend-

**Table 1:** Comparison between the opiate group and the ‘other opioids’ group regarding fulfilled opioid dependence diagnosis and severity of such diagnosis, *i.e.* number of lifetime criteria fulfilled

	Opiate group n=69	Other opioids group n=30
Opioid dependence ICD-10 (F11.2), Lifetime	100 %	100 %
Last 12 months, preceding ORT assessment	99 %	100 %
Severity of opioid dependence, lifetime		
4 criteria	0.0 %	3.3 %
5 criteria	2.9 %	10.0 %
6 criteria	97.1 %	86.7 %

ence diagnoses (ICD-10: F11.2) were met, and to establish whether the number of fulfilled dependence criteria differed between the groups.

In comparing F11.2-diagnosis in the opiate group *vs.* the other opioids group, all or practically all participants in these two groups fulfilled the criteria for opioid dependence both in a lifetime perspective and in the last 12 months preceding the ORT assessment. Most interviewees in both groups met all six criteria, *i.e.* 97 per cent in the opiate group and 87 per cent in the other opioids group. These results established that, in diagnostic terms, the two groups showed opioid dependence of about the same severity, *i.e.* both were shown to have a very serious opioid substance use disorder.

A related problem was whether or not both substance groups had an impact on their development of dependence. Did those in the ‘opiate group’ meet the criteria mainly based on problems incurred from opiate use, and did those in the ‘other opioid group’ meet criteria primarily from their problematic use of other opioids? Or was the development of dependence a process in which both groups of substances played similar roles in the two groups? Table 2 was therefore designed to show, in both groups, the number of criteria for opioid dependence related to problematic use of opiates, *versus* the number of criteria associated with problematic use of other opioids.

There was an expected difference between the groups, *i.e.* the criteria were most often developed in relation to the individual’s favourite drug. We note,

however, that the two groups overlapped to a high degree; 87 per cent and 88 per cent, respectively, of the criteria were met in relation to the other group’s favourite substance, indicating that the categorization in the two groups seemed to be irrelevant to their development of opioid dependence. Most of those in the two groups developed opioid dependence in relation both to opiates and other opioids.

Since polydrug use is common, dependence diagnoses involving substances other than opioids were studied to find out whether one of the two groups had more severe problems of this kind than the other. Table 3 presents other substance dependence diagnoses delivered to members of the two groups, and shows to what extent the dependence diagnoses differed between the two groups.

No differences were detected between the two groups on the issue of lifetime fulfilment of substance dependence in relation to alcohol, sedatives, cannabis, cocaine, amphetamines, hallucinogens, inhalants and polydrug use. It should also be noted that no one in the population received a diagnosis of *harmful use* for any of these substances. They had either developed a dependence diagnosis or had received no diagnosis at all in relation to that substance.

There were no significant differences between the two groups in terms of *the number of* other substance dependence diagnoses. Eight dependence diagnoses in addition to opioids were counted – alcohol, sedatives, cannabis, cocaine, amphetamines, hallucinogens, inhalants and polydrug use (thereby

**Table 2.** Comparison between the opiate group *vs.* the other opioids group regarding lifetime opioid dependence criteria related to opiates and/or to other opioids

	Opiate group n=69	Other opioids group n=30
Opioid dependence criteria in relation to opiates misused	100 %	86.7 %
Opioid dependence criteria in relation to other opioids misused	88.4 %	100 %

**Table 3.** Comparison between the opiate group vs. the other opioids group concerning lifetime dependence diagnosis fulfilled in relation to other drugs

	Opiate group n=69	Other opioids group n=30	P
Dependence diagnoses:			(a)
Alcohol, %	68.1	76.7	0.390
Sedatives, %	84.1	90.0	0.436
Cannabis, %	65.2	46.7	0.084
Cocaine, %	27.5	16.7	0.246
Amphetamines, %	87.0	83.3	0.634
Hallucinogens, %	23.2	13.3	0.262
Inhalants, %	21.7	6.7	0.068
Polydrug, %	63.8	73.3	0.353
Number of dependence diagnoses fulfilled with substances other than opioids (of eight possible),			
m (sd)	4.41 (2.3)	4.07 (1.8)	
md (qd)	5 (2)	4 (1)	0.415 (b)
M (sd) = Mean (standard deviation); Md (qd) = Median (quartile deviation). Significance tested by: a) Chi-2, b) Mann-Whitney U-test.			

ignoring dependence on caffeine and nicotine). The opiate group had a mean of 4.41 and a median of 5, while the 'other opioids' group had a mean of 4.07 and a median of 4. The differences were tested with the Mann-Whitney U-test, but proved not to be significant.

#### 4. Discussion

The results show that all the members of the two groups fulfilled the criteria for severe opioid dependence, both from lifetime and current perspectives. Although the criteria had been developed mainly in relation to dependents' favorite opioid, both opiates and other opioids had substantially contributed to the development of dependence in both groups. Both groups, to the same high degree, also showed that comorbidity in other conditions of substance dependence, including polydrug use, needed to be considered in treatment. None of the participants had received a diagnosis of *harmful use* for any substance, implying that they either received a diagnosis of dependence or else had received no diagnosis at all in relation to the specific substance.

From a previous study [35] on the same population, the two groups examined here also showed similar severity when it came to problems related to overall areas of life. The groups, to the same degree, had major problems in all the areas assessed, which supports the finding that the addictive process was the same in both groups. Many studies, published over time [11, 23, 24, 43, 45] have determined the seriousness of the opioid dependence state; however, no previous study that applied the same categorization

used by the Swedish NBHW (2010) could be found. Other countries include opioid-dependent persons in ORT, regardless of what type of opioid caused the dependence, since all opioids affect the opioid receptors [3, 18, 23, 55].

The World Drug Report [50, 51] as well as other reports [15, 16] and studies [8, 18, 19, 33, 57] note that the use of all types of opioids has increased internationally in the last few decades although there are geographic differences in their distribution patterns [10, 50]. In some of the Swedish cities, *e.g.* Malmö, Stockholm and Norrköping, heroin is the dominant opioid that is misused [6]. Individuals who as adults moved to Jönköping County from those areas – or from other countries where heroin or opium are more commonly misused – used "opiates" to a higher extent. As shown, however, they also used other kinds of opioids at significant levels.

This study has found no evidence in favour of the dichotomic categorization of "opiates" vs. "other opioids", even as a way of defining the severity of opioid dependence. Specialists in pharmacokinetics are familiar with differences between opioids [14], but these differences are not based on that categorization.

When DSM-III was translated into Swedish in 1983, the term 'opioid' was mistranslated by using the Swedish word for opiates, and this mistake was repeated in the later translations of ICD-10 and DSM-IV [37]. These mistakes, and possibly the lack of terminological consistency in international publications, may have contributed to the problematic NBHW statutes in 2010, although this does not explain why the SBU-commented review on the evi-

dence was overlooked. The terminological mistake was corrected in the translation of DSM-5 into Swedish in 2014 [27]. In 2016, the NBHW statutes were changed too, so making it possible for opioid dependents to enter ORT regardless of the type of opioid to be used [40].

As shown in the background, the Swedish ambiguity concerning opiates/opioids is not isolated; it is, in fact, a common finding worldwide. Even the World Drug Report published by the United Nations adds to the confusion by casually shifting between different concepts in the same sentence: “[...] influence on *opioid-dependent* patients in treatment who [...] help control their *opiate dependence* [...]” [50]. Quotations like these emphasize the need for conceptual clarity – a problem highlighted in a *Lancet* editorial published back in 1983: “The painless way to end the abuse and ambiguity is to opt for a uniform terminology. We declare that opioids have won the day”[42]. Unfortunately, the *Lancet* declared this victory at least 34 years too early. We retrospectively commend that urgent plea for more conceptual clarity.

A few limitations to this study need to be mentioned. The population was rather small and was restricted to one county in Sweden. Still, it was a county that had the subpopulations needed for the study, with a well-established distribution of synthetic and other opioids among illicit users, in addition to which heroin and other opiate users migrated to that particular county. The ADDIS interviews were retrospective, to reflect the situation at the time of ORT assessment, which was prior to the new statutes. To prevent recollection bias, all interviews were checked against clinical records and ORT assessment data, which added documentation in support of their validity. There are also strengths to be mentioned, namely using ADDIS as a valid structured instrument for diagnostic assessment, and using an updated drug list based on the ATC classification to assess all the substances being misused.

## 5. Conclusions

This study reveals that both types of opioids used, *i.e.* opiates *vs.* other opioids, contribute substantially to the development of opioid dependence, and that ‘opioids’ is an apt term for conveying a unitary diagnostic concept. There were no scientific grounds for treating the two groups differently. The study also calls for a more stringent use of terminology, enabling full accordance with ICD and/or DSM.

## References

1. A.P.A. (2000): Diagnostic and statistical manual of mental disorders: DSM-IV-TR. American Psychiatric Association, Washington, D.C.
2. A.P.A. (2013): Diagnostic and statistical manual of mental disorders: DSM-5. 5th ed. American Psychiatric Association, Arlington, V.A.
3. Australian Department of Health (2014): National Guidelines for Medication-Assisted Treatment of Opioid Dependence 2014. Department of Health, Canberra, Australia.
4. Bailey C.P., Connor M. (2005): Opioids: cellular mechanisms of tolerance and physical dependence. *Curr Opin Pharmacol.* 5(1): 60-68.
5. Brownstein M.J. (1993): A brief history of opiates, opioid peptides, and opioid receptors. *Proc Natl Acad Sci U S A.* 90(12): 5391-5393.
6. CAN (2010): Drogutvecklingen i Sverige [Drug development in Sweden]. CAN [The Swedish Council for Information on Alcohol and Other Drugs], Stockholm.
7. Cicero T.J., Ellis M.S. (2015): Abuse-Deterrent Formulations and the Prescription Opioid Abuse Epidemic in the United States: Lessons Learned from OxyContin. *JAMA Psychiatry.* 72(5): 424-430.
8. Compton W.M., Volkow N.D. (2006): Major increases in opioid analgesic abuse in the United States: Concerns and strategies. *Drug Alcohol Depend.* 81(2): 103-107.
9. Compton W.M., Jones C.M., Baldwin G.T. (2016): Relationship between nonmedical prescription-opioid use and heroin use. *N Engl J Med.* 374(2): 154-163.
10. Connery H.S. (2015): Medication-Assisted Treatment of Opioid Use Disorder: Review of the Evidence and Future Directions. *Harv Rev Psychiatry.* 23(2): 63-75.
11. Connock M., Juarez-Garcia A., Jowett S., Frew E., Liu Z., Taylor R.J. et al. (2007): Methadone and buprenorphine for the management of opioid dependence: a systematic review and economic evaluation. *Health Technol Assess.* 11(9): 1-171, iii-iv.
12. Davis L.J., Hoffmann N.G., Morse R.M., Luehr J.G. (1992): Substance Use Disorder Diagnostic Schedule (SUDDS): The Equivalence and Validity of a Computer Administered and an Interviewer Administered Format. *Alcohol Clin Exp Res.* 16(2): 250-254.
13. Dreifuss J.A., Griffin M.L., Frost K., Fitzmaurice G.M., Potter J.S., Fiellin D.A. et al. (2013): Patient characteristics associated with buprenorphine/naloxone treatment outcome for prescription opioid dependence: Results from a multisite study. *Drug Alcohol Depend.* 131(1): 112-118.
14. Drewes A.M., Jensen R.D., Nielsen L.M., Dronney J., Christrup L.L., Arendt-Nielsen L. et al. (2013): Differences between opioids: pharmacological, experimental, clinical and economical perspectives. *Br J Clin Pharmacol.* 75(1): 60-78.
15. EMCDDA. (2015): European Drug Report 2015: Trends and Developments. Available at:

- <http://www.emcdda.europa.eu/system/files/publications/974/TDAT15001SVN.pdf>, 2015 Accessed November 15<sup>th</sup>, 2016.
16. Executive Office of the President of the United States. (2011): Epidemic: Responding to America's prescription drug abuse crisis. White House, Washington D.C.
  17. Fiellin D.A., Friedland G.H., Gourevitch M.N. (2006): Opioid dependence: rationale for and efficacy of existing and new treatments. *Clin Infect Dis.* 43 Suppl 4: 173-177.
  18. Fischer B., Rehm J. (2007): Illicit opioid use in the 21st century: witnessing a paradigm shift? *Addiction.* 102(4): 499-501.
  19. Fischer B., Rehm J., Patra J., Cruz M.F. (2006): Changes in illicit opioid use across Canada. *Can Med Assoc J.* 175(11): 1385-1385.
  20. Gerdner A., Wickström L. (2015): Reliability of ADDIS for diagnoses of substance use disorders according to ICD-10, DSM-IV and DSM-5: test-retest and inter-item consistency. *Subst Abuse Treat Prev Policy.* 10(1): 1.
  21. Gerdner A., Kestenberg J., Edvinsson M. (2015): Validity of the Swedish SCID and ADDIS diagnostic interviews for substance use disorders: Sensitivity and specificity compared with a LEAD golden standard. *Nord J Psychiatry.* 69(1) :48-56.
  22. Gilson A.M., Ryan K.M., Joranson D.E., Dahl J.L. (2004): A reassessment of trends in the medical use and abuse of opioid analgesics and implications for diversion control: 1997–2002. *J Pain Symptom Manage.* 28(2): 176-188.
  23. Government of New Zealand. (2014): New Zealand Practice Guidelines for Opioid Substitution Treatment 2014. Ministry of Health, Wellington.
  24. Grönbladh L., Öhlund L.S., Gunne L.M. (1990): Mortality in heroin addiction: impact of methadone treatment. *Acta Psychiatr Scand.* 82(3): 223-227.
  25. Harm Reduction International.(2016): The global state of harm reduction 2016. Harm Reduction International, London. Available at: [https://www.hri.global/files/2016/11/15/Global\\_Overview\\_2016.pdf](https://www.hri.global/files/2016/11/15/Global_Overview_2016.pdf) Accessed November 28<sup>th</sup>, 2016.
  26. Herlofson J. (1984): MINI-D: diagnostiska kriterier enligt DSM-III [MINI-D: diagnostic criteria according to DSM]. Stockholm: Pilgrim Press.
  27. Herlofson J. (2014): Mini-D 5: diagnostiska kriterier enligt DSM-5 [Mini-D 5: diagnostic criteria according to DSM-5]. Stockholm: Pilgrim Press.
  28. Johnson B., Hagström B. (2005): The translation perspective as an alternative to the policy diffusion paradigm: The case of the Swedish methadone maintenance treatment. *J Soc Policy.* 34(3): 365-388.
  29. Jones C.M., Paulozzi L.J., Mack K.A. (2014): Sources of prescription opioid pain relievers by frequency of past-year nonmedical use: United states, 2008-2011. *JAMA Intern Med.* 174(5): 802-803.
  30. Kieffer B.L., Evans C.J. (2002): Opioid Tolerance–In Search of the Holy Grail. *Cell.* 108(5): 587-590.
  31. Krikorian A.D. (1975): Were the opium poppy and opium known in the ancient Near East? *J Hist Biol.* 8(1): 95-114.
  32. Lankenau S.E., Schrage S.M., Silva K., Kecojevic A., Bloom J.J., Wong C. et al. (2012): Misuse of prescription and illicit drugs among high-risk young adults in Los Angeles and New York. *J Public Health Res.* 1(1): 22-30.
  33. Lin L.A., Walton M., Blow F. (2015): Prescription opioid misuse among youth in primary care: A comparison of risk factors. *Drug Alcohol Depend.* 146: 180.
  34. Mattick R.P., Breen C., Kimber J., Davoli M. (2009): Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane Database Syst Rev.* 2009(3): CD002209.
  35. Monwell B., Bülow P., Gerdner A. (2016): Type of opioid dependence among patients seeking opioid substitution treatment: are there differences in background and severity of problems? *Subst Abuse Treat Prev Policy.* 11(1): 23.
  36. Monwell B., Blix O., Gerdner A., Bülow P. (2016): Drug List as a Cognitive Support to Provide Detailed Information on a Patient's Drug Use: A Comparison of Two Methods Within the Assessment of Drug Misuse and Dependence. *Substance Use and Misuse.* 51(11): 1470-1476.
  37. Monwell B., Johnsson B., Gerdner A. (2015): Opiater eller Opioider? Dags att städa bland begreppen. [Opiates or Opioids? Time to clean up among the concepts.] *Lakartidningen.* 112: DRTP.
  38. National Board of Health and Welfare. (2010): Svensk Författningssamling SOSFS 2009:27(M)[Code of Statues SOSFS 2009:27(M)]. NBHW, Stockholm.
  39. National Board of Health and Welfare.(2007): Konsekvensutredning enligt 4 § förordning (2007:1244) om konsekvensutredning vid regelgivning - revidering av Socialstyrelsens föreskrifter och allmänna råd (2004:8) om läkemedelsassisterad behandling av opiatberoende [Consequence assessment according to § 4 legislation (2007:1244) on assessment of consequences of regulatory decisions – revision of The Regulations and Guidelines of the National Board of Health and Welfare (2004:8) concerning medication-assisted treatment of opiate dependence]. NBHW, Stockholm.
  40. National Board of Health and Welfare. (2015): Nationella Riktlinjer: Vård och stöd vid missbruk och beroende - Stöd för styrning och ledning 2015 [National Guidelines: Care and support in case of Misuse and Dependence – Support for governance and management 2015]. Available at: [www.socialstyrelsen.se/Lists/Artikelkatalog/Attachments/19770/2015-4-2.pdf](http://www.socialstyrelsen.se/Lists/Artikelkatalog/Attachments/19770/2015-4-2.pdf) Accessed November 15<sup>th</sup>, 2016.
  41. Okie S. (2010): A flood of opioids, a rising tide of deaths. *N Engl J Med.* 363(21): 1981-1985.
  42. Opiates or opioids? (1983). *Lancet.* March 26(1):687. (Editorial)
  43. O'Shea J., Law F., Melichar J. (2009): Opioid dependence. *Clin Evid.* (24): 1015.

44. Potter J.S., Marino E.N., Hillhouse M.P., Nielsen S., Wiest K., Canamar C.P. et al. (2013): Buprenorphine/naloxone and methadone maintenance treatment outcomes for opioid analgesic, heroin, and combined users: findings from starting treatment with agonist replacement therapies (START). *J Stud Alcohol Drugs*. 74(4): 605-613.
45. Praveen K.T., Law F., O'Shea J., Melichar J. (2011): Opioid dependence. *BMJ Clin Evid*. 2011: 1015.
46. Raisch D.W., Fye C.L., Boardman K.D., Sather M.R. (2002): Opioid dependence treatment, including buprenorphine/naloxone. *Ann Pharmacother*. 36(2): 312-321.
47. SBU Kunskapscentrum för hälso- och sjukvården [SBU Swedish Agency for Health Technology Assessment]. (2007): Behandling av opioidmissbruk med metadon och buprenorfin (Subutex) [Treatment of opioid dependence with methadone and buprenorphine (Subutex)]. Available at: <http://www.sbu.se/sv/Publicerat/Kommentar/Lakemedel-mot-heroinmissbruk--behandling-med-metadon-och-buprenorfin/> Accessed November 15<sup>th</sup>, 2016.
48. Selin J., Perälä R., Stenius K., Partanen A., Rosenqvist P., Alho H. (2015): Opioid substitution treatment in Finland and other Nordic countries: Established treatment, varying practices. *Nordisk Alkohol Nark*. 32(3): 311-324.
49. Vendramin A., Sciacchitano A. (2010): On opioid receptors. *Europad*. 12(4): 23-32.
50. United Nations Office on Drugs and Crime (UNODC). (2016): World Drug Report, 2016. UNODC, Vienna. 2016: 174.
51. United Nations Office on Drugs and Crime (UNODC). (2015): World Drug Report, 2015. UNODC, Vienna. 2015: E.15.XI.6.
52. WHO. (2009): International statistical classification of diseases and related health problems: ICD-10. WHO, Geneva.
53. WHO. (2006): The anatomical therapeutic chemical classification system with defined daily doses (ATC/DDD). WHO, Oslo.
54. WHO. (2009): Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence. Available at: [http://whqlibdoc.who.int/publications/2009/9789241547543\\_eng.pdf](http://whqlibdoc.who.int/publications/2009/9789241547543_eng.pdf). Accessed on November 15<sup>th</sup>, 2016.
55. Wu L.T., Woody G.E., Yang C., Blazer D.G. (2011): How do prescription opioid users differ from users of heroin or other drugs in psychopathology: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *J Addict Med*. 5(1): 28-35.
56. Zacny J., Bigelow G., Compton P., Foley K., Iguchi M., Sannerud C. (2003): College on Problems of Drug

Dependence taskforce on prescription opioid non-medical use and abuse: position statement. *Drug Alcohol Depend*. 69(3): 215-232.

#### Acknowledgements

None

#### Role of the funding source

Authors state that this study was financed with internal funds. No sponsor played a role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

#### Contributors

All authors were involved in the study design, had full access to the survey data and analyses, and interpreted the data, critically reviewed the manuscript and had full control, including final responsibility for the decision to submit the paper for publication.

#### Conflict of interest

All authors have no conflict of interest.

#### Ethics

Authors confirm that the submitted study was conducted according to the WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. The study has been subjected to ethical review and was approved by the Regional Ethical Review Board in Linköping, 2011-06-15 (2011/214-31). All patients gave their informed consent to the anonymous use of their clinical data for this independent study.

#### Note

It is the policy of this Journal to provide a free revision of English for Authors who are not native English speakers. Each Author can accept or refuse this offer. In this case, the Corresponding Author accepted our service.