



Nicotine Dependence Predicts Repeated Use of Prescribed Opioids. Prospective Population-based Cohort Study

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PURPOSE: The aim of this study was to evaluate prospectively smoking dependence as a predictor of repeated use of prescribed opioids in non-cancer patients.

METHODS: We conducted a prospective population-based study cohort of 12,848 men and 15,894 women 30–75 years of age in health surveys in Norway during 2000–2002 with repeated opioid prescriptions (12+, during 2004–2007) recorded in the Norwegian Prescription Database as the outcome measure. Information on history of smoking and potential confounders was obtained at baseline by self-administered questionnaires. For smoking, participants were divided into categories: never; previously heavy (stopped maximum of 5 years earlier; 10+ cigarettes daily); daily not heavy (1–9 cigarettes); dependent daily smokers (10+ cigarettes), and other (previously and/or not daily). Odds ratios (ORs) with 95% confidence intervals (CIs) were estimated by logistic regression.

RESULTS: During follow-up, 335 (1.5%) of survey participants were registered with 12+ prescriptions of opioids during the period 2004–2007. The prevalence of repeated prescription frequency of opioids was higher for men and women with a history of smoking. The adjusted OR for prescribed opioids for dependent daily smokers was 3.1 (95% CI: 2.3–4.1), for daily non-heavy smokers 1.8 (1.2–2.7), and for previous heavy smokers 1.8 (1.1–3.0), compared with never-smokers as reference.

CONCLUSIONS: Results of the study suggest that smoking dependence may predict more frequent use of opioids.

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INTRODUCTION

Opioid analgesics are widely accepted for the treatment of severe acute pain and chronic pain related to active cancer (1–3). In contrast, the repeated use of opioid therapy to treat other types of chronic pain remains controversial (4). Optimal use of opioids should balance the benefits with the risk of problematic use of opioid analgesics. Opioids should be avoided in patients with personal or family history of alcohol or drug abuse. Younger age, presence of psychiatric conditions, and a history of legal problems are also associated with aberrant drug-related behaviors (5–7).

Use of repeated opioid therapy for chronic non-cancer pain has increased substantially (8–10). In the United States, approximately 3.6% of the general population without cancer used opioids several times a week for a month or more in 2001 (10). Central risk factors can increase a patient's likelihood of escalating use of opioids prescribed

for chronic pain and may increase the risk of aberrant behaviors. However, the epidemiology of opioid-taking behaviors in a non-cancer general population has not been fully investigated (11).

Smoking has complex effects on pain perception in humans. Smoking is a risk factor for a number of painful conditions, including low back pain and musculoskeletal pain (12, 13). Smokers also report more frequent requirements for postoperative opioids (13). Results from experimental studies of anti-nociception in mice indicate that possible mechanisms of nicotine's influence on opioid use; nicotine pretreatment induces cross-tolerance to morphine (14), indicating the need of higher opioid doses to achieve the same antinociceptive effect as can be achieved in non-tolerant animals.

There is also another mechanistic possibility on how nicotine might influence later opioid use. Behavioral animal studies have shown that both the rewarding and the psychomotor-activating effects of morphine were enhanced following nicotine treatment (15–17). Nicotine's influence on opioid reward and reinforcement has also been observed in humans, in whom nicotine treatment increased methadone self-administration (18).

Numerous population studies have reported a strong dose-response relationship between cigarette consumption

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Selected Abbreviations and Acronyms

OR = odds ratio

CI = confidence interval

NorPD = Norwegian Prescription Database

CONOR = Cohort of Norway

and severe disease and mortality (19, 20). Cigarette smoking is highly prevalent among individuals with chronic pain (21). There are few longitudinal population-based studies on risk factors and the use of legal prescribed opioids. Most studies have had a cross-sectional design and they have often been conducted on selected patient groups (21, 22). More data on opioid use in the general population are required to determine the factors that may increase unfavorable use in patients with chronic, nonmalignant pain.

The aim of our study was to determine the risk of later repeated opioid use in a general population, in men and women with different levels of smoking at baseline. We report on nearly 30,000 Norwegian adults, aged 30–77 years, who in during the period 2000–2002 participated in health surveys. They were then followed up throughout 2004–2007 for their use of opioids registered in the Norwegian Prescription Database.

MATERIAL AND METHODS

Participants, Health Survey, and Information on Independent Variables

Data from population-based surveys conducted during 2000–2002 in five Norwegian counties—Oslo, Oppland, Hedmark, Troms, and Finnmark—are included in this study (23). These counties cover both rural and urban regions. The surveys are part of Cohort of Norway (CONOR) (24). The number of individuals invited and the number of participants in CONOR, as well as the procedures used, have been published elsewhere (24). All subjects in selected age groups were invited to participate in the respective surveys. Herein we present pooled data for the age groups at the time of investigation: 30, 40–41, 45–46, 59–61, and 75–77 years. The attendance rate was 51%.

Exclusions

The following groups were excluded:

- Men and women who did not respond to at least one of the questions (variables/confounders) used in the study. In total, 13,776 men and 17,102 women responded on all (variables/confounders) used in the study.
- Men and women with a history of using opioids at baseline. These exclusions applied to 3.3% ($N = 457$) of the responders among men and 4.9% ($N = 801$) of the

responders among women. Drug use questions consisted of specific questions on the frequency of use of different drug categories during the previous 4 weeks, followed by an open question on drug trade names (23). It was possible to register up to 10 different trade names in the self-administered questionnaire. Opioid users at baseline were defined as individuals who wrote the trade names of opioids used during the previous month.

- Responders who died or emigrated from Norway before 2004 (men: $N = 319$; women: $N = 286$)
- Responders whose drugs were reimbursed for drugs used in the treatment of cancer (men: $N = 152$; women: $N = 121$)

In total, 12,848 men and 15,894 women who did not report using opioids at screening were included in this study.

Categories of Cigarette Consumption

The participants completed a self-administered questionnaire (23). The questionnaire included questions about smoking: “Have you smoked/do you smoke daily?” and “How long is it since you stopped smoking?” The person attending the health surveys reported the actual number of cigarettes smoked per day in a special box in the questionnaire. Participants were divided into four smoking categories: never; previously heavy (stopped a maximum of 5 years earlier; 10+ cigarettes daily); daily, not heavy (1–9 cigarettes); dependent (heavy) daily smokers (10+ cigarettes); and other (previously and/or not daily, smoking cigars/cigarillos/pipe).

Possible Confounding Factors

Potential confounders include self-reported chronic pain, mental distress and self-reported general health, alcohol consumption, educational level and age known to vary between smokers and nonsmokers and shown to be associated with use of opioids in previous cross sectional studies (21, 25, 26). These variables were included in bivariate and multivariate analyses.

The questionnaire included one question about chronic pain: “Have you, during the past year, suffered from pain and/or stiffness in muscles and joints that has lasted for at least 3 months?” Mental distress was measured by the Mental Health Index, previously documented to be highly correlated with validated instruments; Hopkins Symptom Check List and the Hospital Anxiety and Depression Scale (27). The cut-off value of 2.15 was set as the level for mental distress (27). Alcohol use was divided into three categories: teetotaler/seldom users; alcohol use 1–4 times a month; and several times during one week.

Information about marital status was retrieved from the Norwegian Person Registry.

Norwegian Prescription Database (NorPD): Information on End Point

Prescription data about opioids during 2004–2007 were drawn from the NorPD, which covers the entire nation (4.7 million inhabitants). From January 1, 2004, all pharmacies in Norway have been legally obliged to send in electronic data on all prescriptions. NorPD contains information on all individuals living outside institutions who have received prescription drugs dispensed at pharmacies (28). All prescriptions from ambulatory care, whether publicly reimbursed or not, are stored in the database. The drugs are classified according to the Anatomical Therapeutic Chemical (ATC) classification (29). The data collected include the following: the date the drug was dispensed, ATC code, and defined daily dose. The reimbursement code is also recorded and may be used as a proxy for diagnosis. Code §9.9 is dedicated to cancer diseases.

The opioids were defined by the ATC code N02A in the ATC classification system (29). The weak opioids used in Norway are codeine, dextropropoxyphene, and tramadol; the remaining opioids (ketobemidone, morphine, fentanyl, buprenorphine, hydromorphone, oxycodone, pethidine, pentazocine) are categorized as strong opioids. Opioid formulations marketed for indications other than pain (codeine as a cough suppressant) are not classified in the same ATC group as opioid analgesics and are not included in the analyses.

Repeated prescription frequency of opioids was defined as at least 12 prescriptions of opioids dispensed to individual patients during 2004–2007.

Data from the health surveys and NorPD were linked using the unique 11-digit identification number, assigned to all individuals living in Norway. The record linkage was approved by the Norwegian Data Inspectorate.

Statistical Analysis

Odds ratios (ORs) with 95% confidence intervals (CIs) were estimated by logistic regression. All analyses were carried out by means of SPSS 15.0 for Windows. The level of significance was set to $p < 0.05$. Testing for interaction between smoking and chronic pain, alcohol use, and mental distress was carried out using likelihood ratio testing in a model with and without an interaction term, for men and women combined. We also ran logistic regression on strata for all confounders.

RESULTS

Table 1 shows baseline characteristics of the study population. Dependent daily smokers had the highest prevalence of persons with chronic pain and mental distress. They

also had the highest prevalence of unmarried individuals and of people with lower levels of education.

A total of 335 (1.5%) of survey participants were registered as receiving 12+ prescriptions of opioids during 2004–2007. The prevalence of 12+ prescriptions of opioids 4–7 years after baseline was higher for men and women with a history of smoking (Table 2). Weak opioids dominated and were dispensed in 97.6% of all opioid prescriptions.

The unadjusted OR for later being a repeated user of prescribed opioids was 3.4 for individuals who smoked 10 or more cigarettes daily at baseline (dependent daily smokers) compared to never-smokers (see Table 2). Adjustment for other confounders gave minor changes for risk estimates. There were no interactions between smoking and: sex, mental distress, or alcohol use. ORs between baseline smoking characteristics and later moderate to high prescription frequency of opioids (12+) stratified by chronic pain are presented in Table 3. For both groups, chronic and non-chronic pain, ORs between dependent daily smoking and later moderate to high prescription frequency of opioids were above 2.5.

When one or more prescriptions (1+) of opioids were used as the outcome measure, we observed weaker association between smoking categories and later use of opioids. Adjusted OR for at least one prescription of opioids was 1.6 (95% CI: 1.4–1.7) for dependent daily smokers, 1.2 (1.1–1.4) for daily non-heavy smokers, 1.4 (1.2–1.6) for previous heavy smokers, compared with never-smokers as reference.

DISCUSSION

In this prospective population-based study, there was a dose-response relationship between smoking and subsequent moderate/high frequency of opioid use some years later. The study suggests that the probability of being prescribed opioids is associated with previous smoking dependence independently of the patient's reported chronic pain.

Strengths and Weaknesses

Our study is prospective, using an endpoint recorded in a national health registry. This method gives a minimal risk of selection or information bias. However, although many potential confounders were registered at baseline, it is not possible to take all confounders into account. For example, we do not know the indication for the prescription of opioid analgesics. The initial information on drug use at baseline was self reported and only covered the previous 4 weeks. Furthermore, we do not know if the drugs dispensed are used.

It could be argued that the participants' smoking habits may have changed since the screening took place 4 to 7 years before the endpoint was recorded. Any change in smoking

TABLE 1. Baseline characteristics by smoking groups of 12,848 men and 15,894 women included in the study: Smoking groups by cigarette consumption and history of smoking recorded at screening (2000–2002)

	Smoking group 2000–2002				
	Never	Previously heavy*	Daily (1–9 c)	Dependent daily (10+ c)	Other [†]
Men					
N	5272	901	872	2372	3431
Chronic pain (%)	24.7	33.9	29.7	35.1	32.8
Mental distress (%)	6.4	9.7	9.3	11.3	6.7
Poor/not very good self-reported health (%)	13.1	23.1	19.3	23.3	22.0
Alcohol consumption					
Teetotaler/seldom	20.9	13.5	20.8	17.5	21.7
1–4 times/mo	57.7	55.7	53.0	55.8	48.7
Several times a week	21.8	28.7	26.3	26.8	29.6
Unmarried/no partnership (%)	45.8	49.2	46.9	51.9	29.7
Educational level ≤13 yr (%)	39.5	55.4	59.2	70.1	59.9
Age > 50 yr	26.0	30.1	38.2	28.6	61.3
Women					
N	7166	759	1546	2861	3562
Chronic pain (%)	36.5	40.7	40.1	43.7	41.8
Mental distress (%)	8.3	14.5	11.8	16.4	8.8
Poor/not very good self-reported health (%)	21.0	23.8	21.0	27.6	23.8
Alcohol consumption					
Teetotaler/seldom	37.7	30.4	26.5	26.1	25.4
1–4 times/mo	49.6	53.0	57.8	54.1	52.7
Several times a week	12.7	16.6	15.7	19.8	22.0
Unmarried/no partnership (%)	44.1	57.2	53.4	59.3	42.1
Educational level ≤13 yr (%)	46.3	52.4	60.2	66.9	55.8
Age > 50 yr	36.1	20.2	23.3	24.1	41.2

c = cigarettes.

*Previously heavy: Stopped a maximum of 5 years earlier; 10+ cigarettes daily.

[†]Other: previously and/or not daily; smoking cigars/cigarillos/pipes.

habits, however, would be likely to move toward the null as the prevalence of smoking has decreased in Norway during this period.

No evaluation of non-attendees at baseline was performed in this study, and it is possible that the most frequent drug users or even drug abusers are to be found among the non-attenders. Selection bias due to low participation is a major concern in modern health surveys. The overall response rate in this study was 51%. Non-response will probably affect the prevalence estimates of smokers at baseline. However, it is less likely that the estimate of the relationship between smoking and later opioid use will be affected. This study included only data on drug use from ambulatory care, as NorPD does not include person-specific data from inpatient care. Because our study has a maximum age for participants of less than 77 years, this bias will be small, except for the oldest age group, which will be above 80 years during follow-up. The dose-response relationship between the frequency of cigarette smoking and total mortality has been documented (19). Excluding those individuals who died between baseline and the establishment of NorPD in January 2004 will probably affect the estimates of association. As smokers have higher mortality than non-smokers, the bias will be toward the null.

Opioids may cause cognitive and psychomotor impairment and are potential drugs of abuse (30, 31). However, 12 or more prescriptions of opioids over 4 years are not necessarily a problematic use of opioids and do not indicate abuse or addictive use per se. It was not the intention of this study to investigate predictors of opioid addiction.

Strengths and Weaknesses in Relation to Other Studies

We are not aware of other longitudinal studies in the general adult population that are able to examine risk factors and adjust for confounding variables which were registered before opioids were prescribed. Most studies on risk factor of use of legal prescribed opioids have had a cross-sectional design, in which patients with chronic pain are investigated (22). Cross-sectional studies are limited in their ability to delineate causal connections between any predictors and opioid misuse and abuse behaviors. Use of prescribed opioids has often been based on self-reported use of the drug. In most of the studies, smoking was only investigated as a confounding variable; however, some studies reported that cigarette smoking co-occurs with use of opioids (32, 33). Another problem in many of the earlier studies is that they have used crude measures of smoking patterns without

TABLE 2. Prevalence and adjusted odds ratio of receiving a moderate/high prescription frequency* of opioids by smoking at baseline

	Prevalence No. (%)	Unadjusted odds ratio	Adjusted odds ratio [†] (95% CI)
Smoking			
Never (referent)	87 (0.7)	1	1
Previously heavy**	20 (1.2)	1.7	1.8 (1.1–3.0)
Daily (1–9 c)	34 (1.4)	2.0	1.8 (1.2–2.7)
Dependent daily (10+ c)	124 (2.4)	3.4	3.1 (2.3–4.1)
Other [‡]	70 (1.0)	1.4	1.1 (0.8–1.6)
Sex			
Male (referent)	110 (0.9)	1	1
Female	225 (1.4)	1.7	1.4 (1.1–1.7)
Chronic pain			
No (referent)	100 (0.5)	1	1
Yes	235 (2.3)	4.41	2.5 (1.9–3.2)
Mental distress			
No (referent)	256 (1.0)	1	1
Yes	79 (3.0)	3.1	1.6 (1.2–2.1)
Self-reported health			
Good/very good (referent)	134 (0.6)	1	1
Poor/not very good	201 (3.3)	5.8	2.7 (2.1–3.5)
Alcohol use			
Teetotaler/seldom (referent)	132 (1.7)	1	1
1–4 times/month	149 (1.0)	0.5	0.8 (0.6–1.3)
Several times/week	54 (0.9)	0.6	0.9 (0.7–1.2)
Married/partner			
Yes (referent)	151 (1.0)	1	1
No	184 (1.4)	1.5	1.4 (1.1–1.7)
Educational level			
> 13 yr (referent)	73 (0.5)	1	1
≤13 yr	262 (1.7)	3.2	1.6 (1.2–2.1)
Age			
30 (referent)	41 (0.6)	1	1
40–41 or 45–46	110 (0.9)	1.4	1.1 (0.7–1.6)
59–61	83 (1.3)	2.1	1.3 (0.8–1.9)
75–77	101 (2.8)	4.5	3.1 (2.1–3.5)

CI = confidence interval; c = cigarettes.

*Moderate to high prescription frequency of drug was defined as at least 12 prescriptions of opioids during study period 2004–2007.

[†]Adjusted for smoking, sex, chronic pain, mental distress, self-reported health, alcohol, civil status, educational level, and age.

**Previously heavy: Stopped maximum of 5 years earlier; 10+ cigarettes daily.

[‡]Other: (previously stopped and/or 5 not daily; smoking cigars/cigarillos/pipes).

differentiating between non-dependent and nicotine-dependent/heavy smokers (25).

In a cross-sectional study by Ekholm et al. (21), chronic pain was associated with a slightly higher risk of being a daily and heavy smoker. However, in patients with chronic pain who were treated with opioids, the smoking risk was twice as high as in respondents without chronic pain (21). The study by Tetrault et al. (34) provides only limited support for the smoking/opioid association because the association occurred only in women, but the study investigated non-medical use of prescription opioids. In one prospective study by Stover et al. (35), opioid prescription among individuals

with work-related back injuries was investigated and workers who reported daily tobacco use were twice as likely to receive an opioid prescription compared with those who did not use tobacco products. In a study by Michna et al. (22), patients treated at a hospital-based pain management center, and who were classified as being at high risk for aberrant drug behavior, had higher frequency of current cigarette smoking compared with those who were at lower risk.

As expected, self-reported chronic pain was a strong predictor of subsequent moderate to high opioid use. A cross-sectional population study from Denmark found a higher proportion of opioid users in groups reporting pain (36). In our study, lower educational level, unmarried/non-partnership status, and receiving disability pension were also predictors for later use of moderate to high amounts of opioids. This is in agreement with what has been documented in earlier cross-sectional studies (36).

Not surprisingly, there was an inverse gradient not only between education and the use of opioids, but also between education and smoking. Information about occupation is lacking, but people with low education may be more likely to have jobs with a higher risk of sustaining occupational or strain injuries that require long-term opioid analgesic use. Thus low education is a possible confounder of the association between smoking and opioid use. Adjusting for education, however, did not influence the odds ratio between smoking and opioid use. Even after adjustment for several possible confounders, the odds ratio relating smoking to the use of opioids was minimally reduced.

Studies have shown that psychiatric patients are more predisposed to pain and that common psychiatric disorders (depression and anxiety) may predict initiation and continuation of opioid use in patients with chronic pain (26). A number of epidemiological studies show that mental health problems, in particular depression and anxiety, co-occur with cigarette smoking (37). In our study, we have controlled for mental distress at baseline, which was shown to be an independent strong predictor for later use of moderate to high amounts of opioids.

One-year periodic prevalence shows that 9.4% of the Norwegian population was dispensed at least one opioid analgesic for non-cancer-related pain in 2005 (38). Use of strong opioids is less common among non-cancer patients. In Norway, there is a high consumption of codeine (39). Other weak opioids for the treatment of moderate pain are tramadol and dextropropoxyphene, but they are less frequently used in Norway (38). Our earlier prospective study on codeine use in Norway in 2005 showed that codeine use in the entire Norwegian population was mainly sporadic, but that a relatively large subgroup of users were dispensed repeated prescriptions of the drug in combination with other potential drugs of abuse, such as benzodiazepines

TABLE 3. Prevalence and adjusted odds ratio of receiving a moderate/high prescription frequency of opioids by smoking at baseline stratified by chronic pain

	Moderate to high frequency of opioid prescriptions 2004–2007*			
	No chronic pain		Chronic pain	
	Prevalence No. (%)	Adjusted odds ratio (95% CI) [†]	Prevalence No. (%)	Adjusted odds ratio (95% CI) [†]
Smoking				
Never (referent)	29 (0.3)	1	58 (1.5)	1
Previously heavy**	7 (0.7)	2.2 (0.9–5.1)	13 (2.1)	1.7 (0.9–3.1)
Daily (1–9 c)	18 (1.2)	3.1 (1.7–5.6)	16 (1.8)	1.2 (0.7–2.1)
Dependent daily (10+ c)	30 (1.0)	2.6 (1.5–4.6)	94 (4.5)	3.2 (2.2–4.6)
Other [‡]	16 (0.4)	0.8 (0.6–1.6)	54 (1.2)	1.2 (0.8–1.8)

CI = confidence interval; c = cigarettes.

*Moderate to high prescription frequency of drug was defined as at least 12 prescriptions of opioids during study period 2004–2007.

[†]Adjusted for sex, mental distress, self-reported health, alcohol, civil status, educational level, and age.

**Previously heavy: (stopped a maximum of 5 years earlier; 10+ cigarettes daily).

[‡]Other: (previously and/or not daily, smoking cigars/cigarillos/pipe).

and carisoprodol (39). This combined use may be an indication of problematic drug use.

Mechanisms

There is ample evidence from experimental studies that nicotine and opioids modulate each other's effects. In humans, it has been shown that nicotine gum increased methadone self-administration (18). Behavioral animal studies have shown that both the rewarding and the psychomotor-activating effects of morphine were enhanced following nicotine treatment (16, 17). This phenomenon, referred to as sensitization, is thought to play an important role in the psychopathology of drug abuse as well as in the reinstatement of compulsive drug-seeking behavior (40). The reinforcing and stimulatory effects of both nicotine and opioids are closely related to their ability to increase dopamine in the nucleus accumbens (41, 42). Nicotine pretreatment has been shown to augment morphine-induced dopamine release in this area of the brain (43). The effect of morphine on dopamine is thought to be mediated via μ -opioid receptors on GABAergic neurons in the ventral tegmental area (44); nicotine treatment affects GABAergic transmission in the ventral tegmental area and alters GABAergic response to morphine (43). Both the sensitized dopaminergic response and the alterations in the GABAergic system might be linked to the augmented behavioral response to morphine in nicotine-pretreated mice (43).

Smoking has complex effects on pain perception in humans, and smokers report a greater frequency of chronic pain as well as more frequent requirements for postoperative analgesia (45). In a structured review of the epidemiological literature, a positive association between current smoking and nonspecific back pain has been shown, although a causal relationship has not yet been established (12); in addition, possible mechanisms have not been fully examined.

Nicotine itself has analgesic effects and the mechanisms of this analgesia appear to involve several pathways (46). Several small experimental studies have shown that low-dose nicotine administered as a nasal spray or transdermal patches reduced postoperative opiate requirements in non-smokers (47–49). In animal studies, it has been established that similar mechanisms are involved in both morphine- and nicotine-induced antinociception (50). Repeated use of both opiates and nicotine results in the development of tolerance in animals (14). Even more importantly, cross-tolerance develops between nicotine and opioids; in nicotine-tolerant animals, opioids induce less antinociception and vice versa (14). The development of cross-tolerance indicates that chronic nicotine exposure influences pain systems; the fact that cross-tolerance develops between nicotine and morphine might explain the increased need for analgesia in smokers.

Temporal developmental stages in the use of licit, illicit, and medically prescribed psychoactive drugs from adolescence through young adulthood have been proposed (51, 52). Cigarettes have been suggested to represent a “gateway drug”, the use of which may lead to experimentations with illicit drugs and, later in the mid-twenties, to prescribed psychoactive drugs with a focus on minor and major tranquilizers (52).

Finally, during the last two decades, the use of opioids for treatment of chronic non-cancer pain has increased dramatically in many countries. It could be argued that opioids have benefits in the short run, but in the long run may cause harm (53). It is, therefore, important to investigate predictors for moderate to high or long-term use of opioids in non-cancer patients (11).

Possibly, clinicians need also to screen for smoking habits before starting pain treatment with opioids. A central issue when prescribing opioids for chronic non-cancer pain is to balance the risk of development of problematic use of prescription opioids with the benefits of pain relief. Our

study suggests that smoking dependence may predict higher or more frequent use of opioids.

Conflicts of interest: None declared.

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This study was approved by the Norwegian Data Inspectorate.

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