Clinical Pain Research

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# Prevalence of substance use disorder diagnoses in patients with chronic pain receiving reimbursed opioids: An epidemiological study of four Norwegian health registries

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**Abstract**

**Objectives** – Since 2008, patients have had access to reimbursed analgesics, including opioids, for chronic pain in Norway. There is a need for knowledge on the occurrence and trends over time of substance use disorder (SUD) diagnoses among patients who receive reimbursed opioids for chronic pain. The primary aim of this study was to investigate the prevalence of SUD diagnoses in patients with chronic pain using reimbursed opioids from 2010 to 2019 in Norway. The secondary aim was to investigate the prevalence of other mental health diagnoses among those receiving reimbursed opioids in the subgroups with and without SUD diagnoses.

**Methods** – A cross-sectional design utilising data from four Norwegian nationwide registries.

**Results** – The annual number of individuals with SUD diagnoses increased from 377 to 932 from 2010 to 2019, while the annual prevalence of individuals with SUD remained relatively stable at around 5%. There was a higher prevalence for all categories of other mental health diagnoses among individuals with a SUD diagnosis, compared to those without a SUD diagnosis.

**Conclusion** – The prevalence of SUD diagnoses was low in the population using reimbursed opioids for chronic pain in Norway, but the number of patients increased in the study period because the number of individuals receiving reimbursed opioids increased. Patients with a SUD used on average twice the daily doses of opioids compared to patients without a SUD. They were also more likely to have an additional mental health diagnosis.

**Keywords:** chronic pain, prescription opioid, registry-linkage, substance use disorders

## 1 Introduction

Chronic pain is a significant global public health problem, with major implications for both individuals and society [1]. Around 1/3 of the individuals in high-income countries, including Norway, are estimated to suffer from chronic pain [2,3], and in Norway, it is found that about half of all disability cases can be attributed to chronic pain [4].

Chronic pain is a complex condition that is difficult to treat [5,6]. Treatment can include both opioid and non-opioid pharmacological therapies, psychological therapies,

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as well as integrative treatments and procedures [6]. The short-term use of opioids for acute and terminal conditions has traditionally been widely accepted. Still, the role of opioids in chronic pain is controversial due to the risk of severe adverse events like addiction and overdose deaths and a weak evidence base for the analgesic effect of long-term use [7,8]. In the US, the number of opioid prescriptions has increased dramatically since the 1990s, and the number of opioid-related deaths has increased to over 70,000 deaths a year in 2020 [9].

Several reviews have shown that the most important and consistent risk factor associated with problematic opioid use in chronic pain patients is a past or present opioid or other substance use disorder (SUD) [10,11]. Prescription opioid misuse and addiction among chronic pain patients have been pointed to as an emerging public health concern. A systematic review of 38, mainly US, studies showed an opioid misuse rate of 21–29% and an addiction rate of 8–12% in patients with chronic pain [8]. In comparison, the prevalence of opioid dependence in the general population worldwide is found to be 0.2%, with a higher prevalence in Australia (0.46%), Western Europe (0.35%), and North America (0.3%) [12].

In Norway, drugs can be reimbursed for predefined chronic conditions in need of long-term (at least 3 months) drug treatment. Chronic pain is one such condition that may qualify for reimbursed drugs and therefore a specific reimbursement scheme for the treatment of non-malignant, chronic pain was established in Norway in 2008. The scheme arrangement implied that patients suffering from chronic pain could receive reimbursed analgesics, including opioids for the treatment of moderate to severe chronic pain regardless of the underlying diagnosis. To be eligible for reimbursed opioids, the patient's pain and risk of addiction should be carefully assessed, a concrete treatment plan should be established, and at least two different non-opioids should have been tried without satisfactory effect. Initially, only physicians at pain clinics could prescribe reimbursed opioids. From 2016, general practitioners in Norway were also allowed to apply for approval of reimbursed opioids for specific patients, on the above-mentioned criteria [13].

After 2008 there has been a prominent increase in the number of chronic pain patients using reimbursed opioids in Norway [14], where a high proportion continue to use reimbursed opioids over many years and the prescribed amounts are considerable [15]. With the increasing use of reimbursed opioids to chronic pain patients, it has been a rising concern that the treatment can result in problematic use. However, there is little knowledge about SUD diagnoses in patients with chronic pain. Moreover, although the comorbidity of chronic pain and psychiatric disorders has been well-established [16], few studies have investigated the prevalence of mental health diagnoses among patients receiving opioids. Therefore, the primary aim of this study was to investigate the prevalence of SUD diagnoses in patients with chronic pain using reimbursed opioids from 2010 to 2019 in Norway. The secondary aim was to investigate the prevalence of mental health diagnoses among those receiving reimbursed opioids in the subgroups with and without SUD diagnoses.

# 2 Methods

## 2.1 Study design

A study using a cross-sectional design was conducted utilising linked data from four Norwegian nationwide registries.

## 2.2 Setting

All residents in Norway (5.348 million people in 2019) have universal health and social insurance coverage, and enrolment is automatic. Reimbursed drugs are usually dispensed for 3 months, and the prescription is valid for 1 year [13].

From 2008, patients suffering from chronic pain could receive reimbursed analgesics after an application from a specialist on a specific reimbursement code (reimbursement code 71). A patient could be prescribed reimbursed non-opioids (e.g., paracetamol, non-steroidal anti-inflammatory drugs, gabapentin, pregabalin, amitriptyline, carbamazepine) or opioids for the treatment of moderate to severe chronic pain [13].

Physicians at pain clinics in Norway can apply for approval of reimbursed opioids of up to 300 mg oral morphine equivalents (OMEQs) per day, whereas general practitioners may apply for approval of reimbursed opioids of up to 100 mg OMEQs per day. Opioids can also be reimbursed for palliative care (reimbursement code 90).

## 2.3 Data sources

All Norwegian citizens have a unique personal identification number (PIN). Data from the national health and population registries can be individually linked via this unique PIN which makes it possible to follow an individual over time and also to combine information from the different registries.

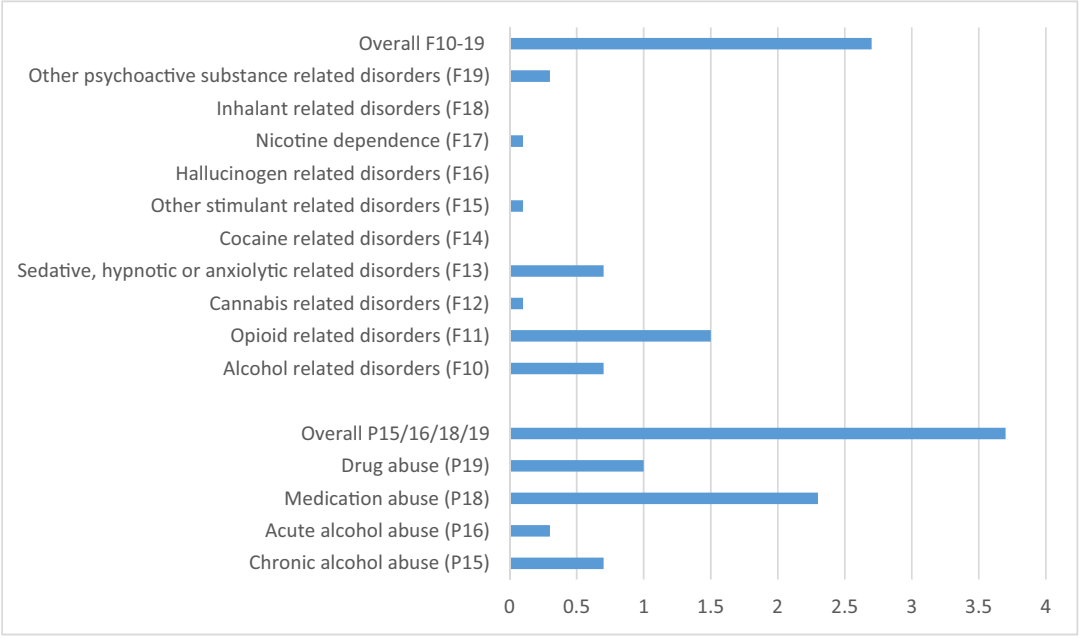


**Figure 1:** Proportion (%) of individuals with different SUD diagnoses in primary and secondary health care among chronic pain patients receiving reimbursed opioids in 2019.

This study utilised data from 2010 to 2019 from four nationwide registries: (1) the Norwegian Prescription Database (NorPD) [17], (2) the Norwegian Patient Registry (NPR) [18], (3) The Norwegian Registry for Primary Health Care (NRPHC) [19,20], and (4) population registries from Statistics Norway [20].

Data on dispensed opioids were drawn from the NorPD [21]. The NorPD contains information on all prescription drugs dispensed from pharmacies to individual patients outside institutions. Each dispensation includes descriptive data such as sex and age, and prescription-related information such as date of dispensation and amount dispensed, as defined daily dose (DDD). Drugs in the NorPD are registered according to the WHO anatomical therapeutic chemical classification system [22].

The NPR [18] is an administrative database of records reported by secondary health care, i.e., all governmental-funded specialised hospitals and outpatient services, including addiction services. The registry covers all public specialist healthcare services in Norway, including private institutions and medical specialists contracted to the regional health authorities. Diagnoses in the NPR are registered with the International Classification of Diseases, 10th revision (ICD-10) codes. In this study, we used data from the NPR on diagnoses reported by hospitals, outpatient specialist clinics, and substance use treatment facilities.

The NRPHC [18,19] is a national database of records reported by primary health care. Diagnoses are registered according to the International Classification of Primary Care, 2nd edition (ICPC-2).

Socioeconomic data such as education and immigrant background were retrieved from the population registries from Statistics Norway [20]. Persons defined as immigrants were born outside of Norway to foreign parents and with foreign grandparents.

## 2.4 Study population

All individuals in Norway 18 years of age and older who filled at least one prescription of an opioid registered with the reimbursement code 71 in the NorPD in the years 2010–2019 were included.

## 2.5 Analysis

We identified chronic pain patients as individuals with at least one filled prescription of opioids with the reimbursement code 71 during each year in the period 2010–2019.

We identified all records of SUD diagnoses registered with the following ICPC-2 codes (primary care): chronic alcohol abuse (P15), acute alcohol abuse (P16), medication abuse (P18), and drug abuse (P19), or with the ICD-10 codes (secondary care): alcohol-related disorders (F10), opioid-

related disorders (F11), cannabis-related disorder (F12), sedative, hypnotic, or anxiolytic related disorders (F13), cocaine-related disorder (F14), other stimulants related disorders (F15), hallucinogen related disorders (F16), inhalant related disorders (F18), and multiple drug use disorder (F19) for each year 2010–2019.

Diagnoses were identified using the first three characters in the code, e.g., F10 for alcohol and related disorders. We calculated the prevalence of any SUD, i.e., at least one registered SUD, for the group of opioid users with the reimbursement code 71 during each year (i.e., annual prevalence).

Next, we investigated the proportion of individuals with different SUD diagnoses for the years 2011, 2015, and 2019 for individuals receiving reimbursed opioids at least once during the actual year. Data for the year 2019 are presented in Figure 1.

Furthermore, we investigated background characteristics and the number and quantity of opioids dispensed and compared the groups with and without SUD among individuals receiving reimbursed opioids at least once during 2019. We also investigated the proportions of individuals in the group with and without SUD who had filled prescriptions for different opioid substances in 2019 (for instance oxycodone and tramadol).

Finally, we investigated differences in mental health diagnoses other than SUDs. Mental health diagnoses registered in primary or secondary care were classified as previously described by Gjerde et al. [16]. We counted mental health diagnoses registered in 2019 for everyone in primary care and secondary care separately. If the same diagnosis was registered at both levels, the diagnosis was only counted once for that individual.

# 3 Results

## 3.1 Prevalence of any SUD diagnosis

The annual prevalence of any SUD diagnosis from 2010 to 2019 among chronic pain patients receiving reimbursed opioids is presented in Table 1. The annual number of patients with any SUD diagnoses increased from 2010 ($N$ = 377) to 2019 ($N$ = 932), while the annual prevalence of patients with SUD remained relatively stable at around 5% throughout the study period.

## 3.2 Prevalence of specific SUD diagnoses

The most frequent SUD diagnoses registered by ICD-10 codes in specialist health care services among individuals receiving reimbursed opioids in 2019 were opioid-related disorders (F11), alcohol-related disorders (F10), and sedative-hypnotic, or anxiolytic-related disorders (F13) with proportions of 1.5, 0.7, and 0.7%, respectively. Correspondingly, medication abuse (P18), drug abuse (P19), and chronic alcohol abuse (P15) were the most frequent SUD diagnoses registered by ICPC-2 codes in primary health care with proportions of 2.3, 1.0, and 0.7% (Figure 1). The same trend was also observed in 2011 and 2015 (results not shown).

## 3.3 Differences in characteristics between individuals with and without SUD diagnosis

The proportion of women receiving reimbursed opioids was higher than the proportion of men in both groups (with SUD diagnoses: 58.5% and without SUD diagnoses: 67.4%), but there were relatively more men in the group with any SUD diagnoses than in the group without such diagnoses (Table 2). In addition, the mean age was lower in the SUD group than in the group without SUDs (53.5 vs 62.6 years). The individuals with a SUD diagnosis received nearly double the amount of opioids compared to those without a SUD diagnosis, both measured as the number of DDDs and the number of filled prescriptions. There were differences in the use of opioid substances between individuals in the group with and without SUD (Figure 2). This was especially prominent for oxycodone where 57.4% of individuals with SUD had filled a prescription of oxycodone compared to 32.4% in the group without SUD. A higher proportion was also observed for the other strong opioids fentanyl and morphine, but not for buprenorphine.

**Table 1:** Number ($n$) and proportion (%) of individuals with and without any SUD diagnosis among patients receiving reimbursed opioids for chronic pain over the years 2010–2019

| Year | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 |
|---|---|---|---|---|---|---|---|---|---|---|
| Without SUD diagnoses, $n$ (%) | 6,500 (94.5) | 7,097 (94.8) | 7,654 (94.7) | 8,266 (94.9) | 8,609 (94.6) | 9,220 (94.7) | 10,200 (94.4) | 15,410 (94.9) | 16,569 (94.7) | 17,615 (95.0) |
| With SUD diagnoses, $n$ (%) | 377 (5.5) | 388 (5.2) | 432 (5.3) | 447 (5.1) | 492 (5.4) | 512 (5.3) | 602 (5.6) | 829 (5.1) | 924 (5.3) | 932 (5.0) |

**Table 2:** Characteristics of individuals with and without SUD diagnoses and amount of opioids prescribed in 2019

| | With SUD diagnoses | Without SUD diagnoses | *p*-value |
|---|---|---|---|
| Total number, *n* | 932 | 17,615 | |
| Women, *n* (%) | 545 (58.5) | 11,855 (67.4) | <0.001 |
| Age, mean | 53.5 | 62.6 | <0.001 |
| **Education**, *n* (%) | | | |
| Primary school/lower secondary school | 400 (42.9) | 6,471 (36.7) | <0.001 |
| Upper secondary school | 401 (43.0) | 7,944 (45.1) | |
| Higher education | 123 (13.2) | 3,012 (17.1) | |
| No data | 8 (0.8) | 188 (1.1) | |
| **Immigrant background**, *n* (%) | | | |
| No | 846 (90.8) | 15,743 (89.4) | 0.177 |
| Yes | 86 (9.2) | 1,871 (10.6) | |
| **Filled prescription of opioids** | | | |
| Quantity of opioids measured as DDD dispensed last year, mean, median (IQR) | 635, 436 (232–760) | 336, 233 (112–431) | <0.001 |
| Number of filled opioid prescriptions during the last year, mean, median (IQR) | 37.7, 29 (16–48) | 16.5, 12 (7–21) | <0.001 |

SUD – substance use disorder, DDD – defined daily dose, IQR – interquartile range.

### 3.4 Differences in mental health diagnoses between individuals with and without SUD diagnosis

As shown in Figure 3, the prevalence of nine out of ten mental health diagnosis categories was significantly ($p < 0.001$) higher in patients receiving reimbursed opioids having a SUD diagnosis compared to those not having a SUD diagnosis. The three most prevalent diagnosis categories were depressive and related mood disorders, sleep disorders, and disturbance, in addition to phobia and other anxiety disorders, with a prevalence of 26.7, 26.6, and 22.3%, respectively, for those having a SUD, and 11.1, 16.2, and 5.9% for those not having a SUD (Figure 3).

## 4 Discussion

Using nationwide and complete registry data, the current study presents a thorough investigation of the annual prevalence of SUD diagnoses amongst individuals treated with reimbursed opioids for chronic pain in Norway. The

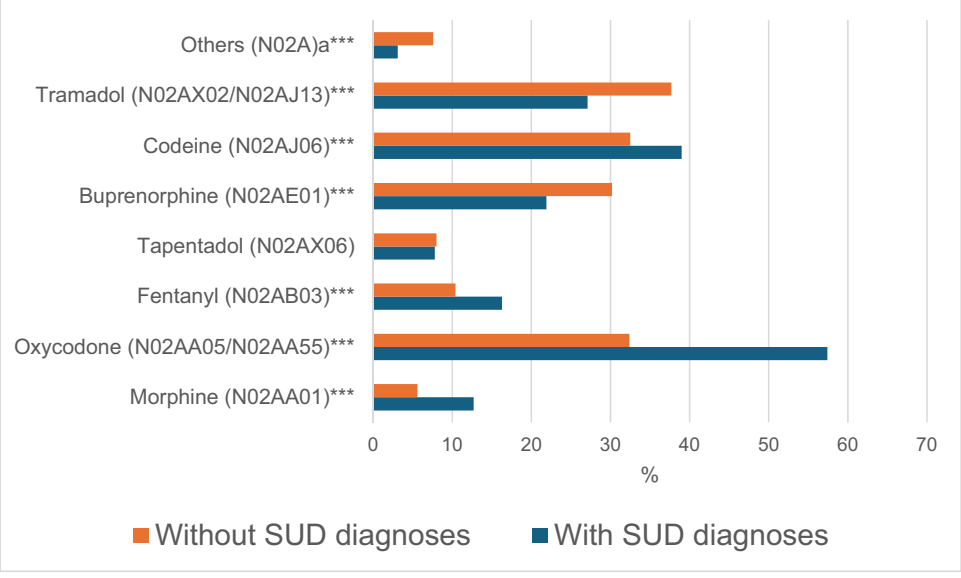


**Figure 2:** The proportion (%) of individuals in the groups with and without SUD who had filled prescriptions for different opioid substances in 2019. a = other opioids than those shown in the figure. *** = $p < 0.001$.

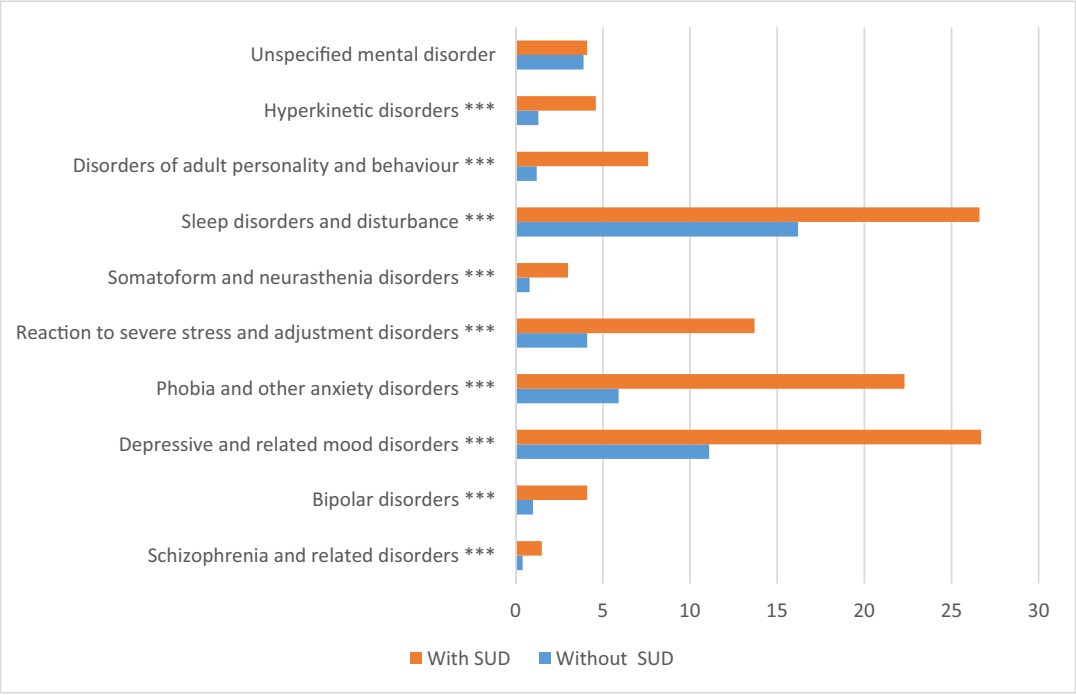


**Figure 3:** Percentage of patients with other mental health diagnoses among patients with and without a SUD diagnosis. Mental health diagnosis categories marked with (***) have a statistically significant difference in the prevalence between the group of patients who have a SUD diagnosis and the group that did not have a SUD diagnosis in 2019 ($p < 0.001$).

accumulated number of individuals with SUD diagnoses increased from 2010 to 2019. Medication abuse diagnoses in primary health care and opioid-related disorder diagnoses in secondary health care were the most prevalent SUD diagnoses and the prevalence of other mental health diagnoses among individuals with SUDs was considerably higher compared to individuals without SUD.

In the current study, the prevalence of SUD diagnoses amongst individuals with chronic pain receiving reimbursed opioids remained stable at around 5% from 2010 to 2019. However, the number of individuals who received reimbursed opioids for chronic pain has increased since the introduction of the reimbursement scheme in 2008 [15]. Because of this, even if the proportion remained stable, the number of individuals receiving an opioid with reimbursement for chronic pain increased from 377 to 932.

Implementing a new reimbursement scheme, as done in Norway in 2008, will naturally lead to an increase in patients being enrolled in the reimbursement scheme over time. Chronic pain patients initiated on opioids often continue to use opioids for many years [15], and if the number of patients using opioids continues to rise, the number of patients with a concomitant substance abuse diagnosis will likely continue to rise as well. This is worrying because having a SUD is found to increase the risk of overdose-related mortality and to be the strongest single risk factor of opioid-related death [23]. Hence, the development of opioid use should be monitored closely in the upcoming years.

A systematic review from 2018 including 38 studies found an average rate of opioid misuse between 21 and 29% and a rate of addiction across studies between 8 and 12% [8]. Also, a recent systematic review and meta-analysis reported a pooled prevalence of 9.3% for dependence and opioid use disorder among patients with long-term non-malignant pain [24]. These findings show higher rates than the 1.5% with opioid-related disorders (F11) in this study. However, various definitions of misuse and addiction, differences in patient populations in the included studies as well as variations in methods used to investigate opioid-related disorders, and observation time in the studies, make it difficult to compare the findings. Notably, in this study, we used national registry data where all patients who received reimbursed opioids for chronic pain in Norway were included, but the prevalence of SUDs was based on the diagnosis codes set by doctors in primary or secondary care. Moreover, a possible reason for the lower prevalence in this study is that the risk of addiction should be assessed before initiating opioid treatment and documented when applying for reimbursement.

Thus, patients receiving reimbursed opioids for chronic pain is a selected population and the prevalence might be lower than in the general population using opioids. Also, we investigated the yearly prevalence of SUD and mental health diagnoses and not lifetime prevalence. Thus, patients might have received such diagnoses during the years before or after being dispensed reimbursed opioids. This might lead to an underestimation of the prevalence in the current study.

The annual prevalence of alcohol-related diagnoses was low with chronic alcohol abuse (P15 in ICPC-2) of 0.7%, acute alcohol abuse (P16 in ICPC-2) of 0.3, and 0.7% for alcohol-related diagnoses (F10 in ICD-10). Careful prescreening of alcohol habits is recommended before initiating long-term opioid use for chronic pain because concomitant use increases the risk of overdose and death [25]. This might be one explanation for the low prevalence of alcohol abuse found in the current study. Another possible explanation might of course be that alcohol abuse is underdiagnosed in these patients.

Nevertheless, it is well established that long-term use of opioids is associated with harmful side effects like addiction, development of tolerance and overdoses [26]. In the current study, the background characteristics of chronic pain patients treated with reimbursed opioids for chronic pain showed that the individuals with SUD were younger and a higher proportion was men compared to the non-SUD group. This adds to other studies showing that women are more likely than men to use opioids for chronic pain, but men are more likely to misuse opioids [27].

An important finding in the current study was the high doses dispensed to the individuals treated with reimbursed opioids who also had SUD. These doses were nearly double the doses dispensed to those without a concomitant SUD diagnosis. Also, the group with SUD received to a larger extent several of the strong opioids, and especially oxycodone. Buprenorphine, which is a strong opioid mainly used in patches, was used more frequently in the group without SUD. One explanation for both the high doses and the type of substances used could be that the patients with a pre-existing SUD have developed a tolerance for opioids and therefore need higher doses and stronger opioids to achieve adequate pain relief. Another explanation is that patients who receive opioids due to reasons such as postoperative pain control might still develop tolerance and iatrogenic misuse over time [28]. Moreover, opioid-addicted patients who for some reason do not qualify for opioid maintenance therapy programmes or drug-assisted rehabilitation programmes might receive high doses of opioid analgesics from their general practitioner as opioid maintenance therapy. Such treatment would be outside the recommendations, but we cannot rule out that this is the case for some patients. Notably, as previously described by others [29,30], there is a group of patients who have severe problems with their opioid use without fulfilling the criteria for an opioid use disorder or addiction criteria but if and how this affected the current study is unknown. Nevertheless, the high doses dispensed to patients with a SUD diagnosis are worrying because higher doses increase the risks of overdose and death.

Finally, our study shows a high prevalence of other mental health diagnoses among individuals with chronic pain who use reimbursed opioids. The prevalence was considerably higher for the individuals who also had a SUD diagnosis for all mental health diagnosis categories. This finding adds to previous studies showing that SUD diagnoses often occur together with mental health disorders [31–35]. In addition, patients suffering from depression are twice as likely to transition to long-term opioid use compared to non-depressed patients [36], and a prevalence of depression of 7% in a general chronic pain population has previously been shown [37]. Previous studies suggest that depression increases the risk of abuse or nonmedical use of opioids, e.g., to treat insomnia [36], and patients who have psychiatric comorbidities and SUD also have a higher risk of opioid-related deaths [23]. Even if guidelines advise clinicians to be restrictive with opioid treatment in this population, this study found that 26% of the individuals with a SUD taking opioids also had a depressive or mood-related disorder and patients taking reimbursed opioids for chronic pain without a SUD diagnosis also had a high prevalence of depressive disorders.

## 5 Strength and limitations

A significant strength of the study is that information about dispensed reimbursed opioids was based on prospectively collected data on dispensed drugs from the NorPD, eliminating the possibility for recall bias and primary non-compliance. Also, the reimbursed prescriptions contained information about the indication of use (reimbursement code 71 for non-malignant, chronic pain). Another strength is the use of diagnosis codes from both primary and specialist care.

The study also has some noteworthy limitations. Since information about opioids was based on filled prescriptions, we do not know whether the patients used the drugs or not. However, these patients received reimbursed prescription drugs, and they filled several prescriptions, increasing the probability that they were consuming the drugs. As the NorPD only contains information about filled prescriptions from pharmacies, individuals living in institutions were not included in

the study population. The DDD was used when analysing opioid consumption. As opposed to strong opioids, the DDD of weak opioids (e.g., codeine, tramadol) is based on the main indication of moderate pain and not severe pain. Therefore, the DDD value of a weak opioid represents a weaker analgesic effect than a DDD of a strong opioid. The DDDs of stronger opioids could also represent different analgesic effects [38], however, to a smaller extent than when comparing weak and strong opioids. As a result, when using DDDs as a measure in drug utilisation studies, especially weak opioids will be overrepresented compared to when using OMEQ which better represents equipotency. If we assume that people with SUD have more frequent use of strong opioids compared to people without SUD, the difference in the amount of opioids used by these two groups would be even greater. Another possible limitation is the possibility of incorrect clinical coding which could reduce the quality of the register data. Since this study had a cross-sectional design, it does not give us the possibility to study if the SUD was diagnosed before or after the reimbursed opioid treatment for chronic pain.

# 6 Conclusions

About 5% of patients who received opioids reimbursed for the treatment of chronic pain also had a SUD diagnosis. The proportion of patients with a SUD diagnosis remained stable over the years from 2010 to 2019, but because the number of patients who received opioids increased, the number of patients with a SUD diagnosis also increased. Patients with a SUD used on average twice the daily doses of opioids compared to patients without a SUD. They were also more likely to have a mental health disorder in addition, most commonly depression, anxiety, or sleep disorders.

**Research ethics:** The research complies with all the relevant national regulations, and institutional policies and was performed by the tenets of the Helsinki Declaration. Approval for the study was obtained from the Regional Committee for Medical Research Ethics South East Norway, REK South East, approval number 2019/656/REK sør-øst C.

**Author contributions:** The authors have accepted responsibility for the entire content of this manuscript and approved its submission. All authors read and approved the final manuscript. THN, SS, IO, LP, PCB and MH took part in the design of the study and the interpretation of the data. SS, IO and MH were responsible for retrieving the data and the first analysis. SS and THN were responsible for writing the first draft of the manuscript.

**Competing interests:** Torunn Hatlen Nøst is an Edior of Scandinavian Journal of Pain (Nursing and Pain Management). The authors state no conflict of interest.

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**Informed consent:** The study only handled anonymised data retrieved from national registries.

**Data availability:** The raw data can be obtained on request from the corresponding author.

**Use of large language models, Artificial intelligence/ Machine learning tools:** Not applicable.

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