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Opioid use disorder in chronic non-cancer pain in Germany: a cross sectional study

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ABSTRACT

Objectives The DSM-5 diagnosis 'opioid use disorder' (OUD) was established to better describe and detect significant impairment or distress related to opioid use. There is no data on rates of OUD in chronic non-cancer pain (CNCP) in European countries. Therefore, our objective was to screen patients in specialised pain centres for signs of OUD.

Design Cross-sectional questionnaire study.

Setting Four outpatient pain clinics in the area of Bonn, Germany.

Participants n=204 patients participated in the study (response rate: 87.9%). All adult patients with opioid pain therapy >6 months for CNCP were included. Excluded were patients with malignant disease, patients who could not collect their prescription themselves due to age or multimorbidity and patients on opioid-maintenance therapy.

Primary and secondary outcome measure Primary outcome measure was the proportion of patients with mild to severe OUD.

Results One-fourth (26.5%) of participants were diagnosed with OUD. Moderate to severe disorder was found in 9.3. Young age was the only connected risk factor (OR 0.96 [95% CI 0.94 to 0.99], p: 0.003).

Conclusions OUD is a relevant diagnosis in patients on long-term opioid therapy for CNCP in the Bonn area. Careful follow-up by the attending physicians is advisable, especially in patients with moderate or severe disorder.

Strengths and limitations of this study

- This study is the first of its kind in Germany and gives a first estimate of the extent of opioid use disorder (OUD) in Germany.
- The response rate was high and non-participants did not differ significantly from participants regarding age and sex.
- The DSM-5 diagnostic criteria are a promising new tool, but only moderate to severe OUD shows good agreement with the ICD-10 and DSM IV definitions of dependence.
- The study was only performed locally.
- Two-thirds of the pain centres in Bonn did not participate, therefore generalisability is limited.

BACKGROUND

Opioids are a cornerstone in the treatment of pain, but like any other potent medication they come with a downside. This downside involves a narrow therapeutic ratio, a lack of documented effectiveness in the treatment of several aspects of chronic non-cancer pain (CNCP) as well as misuse and dependence.[1] The current 'opioid epidemic' in the USA shows the substantial burden of opioid use disorder (OUD) on individuals, their families and society as a whole. Therefore vigilance is needed—but data on OUD while receiving opioid pain therapy in the European Union (EU) is limited.

Data from the European Monitoring Centre for Drugs and Drug Addiction show relatively stable numbers for problematic opioid use as well as overdose deaths throughout the EU between 2000 and 2016.[2] A general population survey with 22 070 participants throughout several European countries showed a past-year prevalence of non-medical prescription opioid use highest in Spain (6.8%) and the UK (6.2%) and lowest in Germany (2.9%).[3] Based on the available data on opioid misuse and addiction in Germany, several experts have concluded that the country is in no apparent danger of an opioid epidemic.[3–6] While prior studies mainly focused on problematic and non-medical use, the prevalence of a defined OUD in the general public as well as in risk groups in Germany has not been investigated. Patients with CNCP on long-term opioid therapy (LTOT) are a prominent example for a risk group for OUD. They are subject to several risk factors for opioid addiction like prolonged exposure to high daily doses of morphine equivalent and psychiatric comorbidities like depression.[7 8] In Germany, 1.3% of the publicly insured are on LTOT, of which 15.5% receive more than 100 mg of morphine equivalent/day.[5] In a prior study,

we were able to show, that the risk of opioid misuse in CNCP on LTOT in general practice is considerable (30.5%).[9]

Currently, significant effort is put into reversing the opioid epidemic in the USA. A new Centers for Disease Control and Prevention guideline for 'Prescribing Opioids for Chronic Pain' puts a special focus on improving doctor's prescription patterns.[1] While this effort is necessary in fighting the epidemic, experts apprehend that they might also result in a repeat 'swing of the opioid pendulum', meaning an undertreatment of opioid sensitive pain types like cancer pain due to an exaggerated fear of opioid addiction.[10] Therefore, the message as well as the wording has to be prudent when commenting on the risk of opioid misuse/dependence during opioid pain therapy.

The diagnosis 'opioid use disorder' might help to achieve an objective approach towards opioid misuse/addiction in Europe. It was first defined in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) in 2013 and replaces the current misuse/dependence dichotomy.[11] Its advantages include:

- OUD represents a continuum of 'mild', 'moderate' and 'severe' and can therefore be of use in monitoring opioid pain therapy.
- OUD and the need for opioid pain therapy may coexist in some patients and do not necessarily exclude each other.
- The absence of negatively charged terms like 'addiction' or 'misuse'.

The diagnosis of OUD (mild, moderate and severe) requires that the individual has significant impairment or distress related to opioid use represented by 2 or more of 11 criteria within a given year.[11 12] For patients under medical supervision, only 9 of the original 11 criteria are applicable. A complete list of all criteria is given in the results section.

The main goal of this study is to determine which proportion of CNCP patients on LTOT in Germany display OUD.

METHODS

We conducted a cross sectional, paper-based questionnaire study at pain clinics in the Bonn area using the new diagnostic criteria for OUD as laid out in the German version of the DSM-5.[11]

Recruitment of participating centres: we contacted all outpatient pain specialists in the greater Bonn area (n=11) as listed by the German medical association via fax, email and telephone. We did not include other medical professions as we could not have controlled for duplicates. We choose specialised pain care, as we expected patients to be under optimal pain therapy in the field and also expected to recruit the highest number of patients on LTOT.

Recruitment of participating patients: All patients on LTOT (>6 months) for CNCP, who entered the offices to collect their prescription, were asked to fill in the questionnaire by the front desk staff. In order to reduce the extra work burden for the doctors as well as social desirability bias, patients filled the information in themselves, without supervision. Front desk staff at all centres was instructed regarding the study protocol and mode of patient selection by the same investigator using a standardised procedure. The study period was 3 months, as it represents the maximum duration of a prescription in Germany, making sure we included all relevant patients. Those who did not want to participate were asked to fill in their age and sex to test for differences in participants and non-participants.

Inclusion criteria were LTOT (>6 months) for CNCP. Excluded were patients with malignant disease, patients who could not collect their prescription themselves due to age or multimorbidity and patients on opioid-maintenance therapy.

When creating the questionnaire, diagnostic criteria were rephrased into concrete questions, keeping them as close to the original wording as possible. All questions are reported in combination with the results in the results section.

As patients were under constant medical monitoring, the criteria 'Tolerance' and 'Withdrawal' (criteria 10 and 11) were not used in diagnosing OUD as defined by the DSM-5 manual. The questionnaire was pretested for comprehensibility and acceptability with five representative patients by our study group, using cognitive interviewing techniques.

Patient and public involvement: the previously mentioned pretest was the first stage of the study in which patients were partly involved. Their comments were used in order to improve comprehensibility and acceptability, methodological aspects and outcome measures were not discussed with patients.

The data management was performed at the Institute of General Practice and Family Medicine in Bonn and included data entry, data validation by plausibility checks, frequency analyses and advanced statistics using IBM SPSS Statistics V.22.

For comparison of age, we used the Mann-Whitney U-test because age showed a not-normal distribution in our sample. For comparison of sex we used the Pearson's χ^2 test. We used exploratory statistics to describe patients' characteristics. A multiple logistic regression model with a dichotomous dependent variable was to explore the relationship between several independent variables and the presence of OUD.

Participants received oral and written information on the study as well as the questionnaire. They were then given the option to put an empty or filled out anonymous questionnaire in a sealed box which was later handed over to the researchers. This procedure was used to give patients the opportunity of non-participation without being revealed. The return of a completed questionnaire was then interpreted as informed consent obtained from participants.

Table 1 Participant characteristic

Participant characteristic	
Age	61.8 (SD: 14.6) (age range 22–92)
Sex: female	64.5% (n=129)
Depression (self-report)	40.6% (n=80)
Education	No school: 1.6% (n=3) Basic compulsory education: 42.0% (n=81) Secondary school or higher: 56.5% (n=109)
Duration of opioid therapy	>6 months: 13.8% (n=26) >12 months: 7.5% (n=14) >18 months: 6.9% (n=13) >24 months: 12.8% (n=24) >48 months: 59.0% (n=111)
Type of pain (multiple answers were possible)	Back pain: 33.8% (n=139) Joint pain: 20.0% (n=82) Neck pain: 11.4% (n=47) Headache: 9.7% (n=40) Postoperative pain: 9.0% (n=37) Rheumatic pain: 6.1% (n=25) Other pain: 10.0% (n=41)

RESULTS

Of the 11 pain specialists we contacted in the greater Bonn area via fax, email and telephone, four offices were willing to participate. Five offices did not respond to our various attempts to contact them. One office refused to participate as they did not approve of our proposed method, another office refused because of holiday hours.

The inclusion criteria were met by n=228 patients from the four outpatient pain centres, a total of n=204 completed the questionnaire (response rate: 87.9%). Four patients had to be excluded later as they did not match inclusion criteria. On average, we received 57 (range: 41–71) questionnaires per office. No drop-outs occurred.

Of the non-participants, 21 out of 24 agreed to have their age and sex documented. Non-participants differed slightly from participants concerning age and sex, without differences being statistically significant

The mean age of participants was 61.8 years (SD 14.6), 64.5% were women. Most participants reported back, joint and neck pain as the reason for taking opioid analgesics. Most participants reported only one or two different types of pain (71%). A total of n=11 patients reported headaches as the single reason for taking opioids, despite the diagnosis being a contraindication for opioid pain therapy. More than half of the participants had been taking opioids for more than 4 years (table 1: participant characteristics).

OUD was diagnosed in 26.5% of patients. The individual percentages for each centre were 22.5%, 37.5%, 21.3% and 32.5%. There was no significant difference found between the four centres concerning percentage of diagnosis of OUD. Absolute and relative numbers including degree of OUD and positive patients per criterion are given in table 2.

The most frequently positive criteria as well as the criterion definition and the questions used are displayed in table 3.

The results of the regression model used to test for correlating factors towards OUD are displayed in table 4. A significant correlation was only found for the variable age. With each additional year of age, the probability of being diagnosed with OUD was reduced by 3%.

We used a multiple regression model to control for statistically significant correlations between the diagnosis OUD and the documented patient characteristics. The model was sound, showing a Nagelkerke's Pseudo-R^2 of 0.271.

DISCUSSION

As a main result of our study, OUD was identified in more than one-fourth (26.5%) of the examined patient group, with 9.3% showing moderate to severe OUD. The response rate was high (87.9%,). Back, joint and neck pain were the most commonly reported reasons for taking opioid painkillers. A statistically significant correlation between young age and OUD was identified.

This study has its strengths and limitations. The study strengths include: that this research was based on a multicentre sample of outpatients, that it was the first of its kind in CNCP patients in Germany and Europe and that OUD was assessed based on the new DSM-5 criteria and therefore displayed in an objective continuum.

Several limitations apply to this study. In terms of generalisability, limitations include that we only approached offices in one area of Germany. Also, we were only able to recruit four out of eleven pain centres which may constitute a selection bias. On the level of individual offices, we recorded a high response rate. Age and sex were similar to comparable populations and did not differ statistically

Table 2 Severity of opioid use disorder and proportion of patients distributed by the number of positive criteria

Severity of OUD	No OUD: 73.5%		Mild OUD: 17.2%		Moderate OUD: 4.4%		Severe OUD: 4.9%			
Number of positive criteria	0	1	2	3	4	5	6	7	8	9
Patient distribution in % (n)	55.4% (113)	18.1% (37)	6.9% (14)	10.3% (21)	1.5% (3)	2.9% (6)	2.4% (5)	1.0% (2)	1.0% (2)	0.5% (1)

OUD, opioid use disorder.

Table 3 Criteria for opioid use disorder, questions used and proportion of positive patients per question

	Opioid use disorder: 'A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following criteria, occurring within a 12 month period.'	n=patients positive per criterion (%)
1	Opioids are often taken in larger amounts or over a longer period of time than intended. *Question 1: Have you taken opioids in larger amounts or over a longer period than intended?*	32 (13.5%)
2	There is a persistent desire or unsuccessful efforts to cut down or control opioid use. *Question 2: Do you have a persistent desire to cut down or control opioid use or have you made unsuccessful efforts to do so?*	47 (19.8%)
3	A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects. *Question 3: Do you spend a great deal of time in activities necessary to obtain the opioid, use the opioid, and/or recover from its effects?*	18 (7.6%)
4	Craving, or a strong desire to use opioids. *Question 4: Do you feel a craving or a strong desire to use opioids?*	35 (14.8%)
5	Recurrent opioid use resulting in a failure to fulfil major role obligations at work, school, or home. *Question 5: Has recurrent opioid use resulted in a failure to fulfil a major role obligation at work, school or home?*	26 (11.0%)
6	Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids. *Question 6: Have you continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids?*	10 (4.2%)
7	Important social, occupational or recreational activities are given up or reduced because of opioid use. *Question 7: Have you given up or reduced important social, occupational or recreational activities because of opioid use?*	34 (14.4%)
8	Recurrent opioid use in situations in which it is physically hazardous *Question 8: Have you used opioids in a recurring manner in physically hazardous situations?*	14 (5.9%)
9	Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by opioids. *Questions 9: Have you continued to use opioids despite the knowledge of having a persistent or recurring physical or psychological problem that is likely to have been caused or exacerbated by opioids?*	21 (8.9%)
10*	Tolerance, as defined by either of the following: ► A need for markedly increased amounts of opioids to achieve intoxication or desired effect. ► A markedly diminished effect with continued use of the same amount of an opioid. (Note: this criterion is not considered to be met for those taking opioids solely under appropriate medical supervision.)	n.a.
11*	Withdrawal, as manifested by either of the following: ► The characteristic opioid withdrawal syndrome (refer to Criteria A and B of the criteria set for opioid withdrawal). ► Opioids (or a closely related substance) are taken to relieve or avoid withdrawal symptoms. (Note: This criterion is not considered to be met for those individuals taking opioids solely under appropriate medical supervision.)	n.a.

2–3 criteria: mild | 4–5 criteria: moderate |≥6 criteria: severe.
*DO NOT apply if opioids are taken as prescribed/under medical supervision.

significant between participants and non-participants.[13] This suggests that a selection bias at an office level is rather unlikely.

In terms of reliability, our survey data were based on patient self-report while technically, DSM-5 criteria should be applied and assessed by a doctor. It is unclear how this setting influenced patients in terms of social desirability. Our approach offered patients full anonymity and gave no disincentives for being honest. Taking into account the high response rate given the controversial topic, we assumed that using self-report has been a viable approach. On the other hand, patients might have misinterpreted some of the questions asked which may have resulted in a considerable bias. Disentangling the negative effects of chronic pain and painkiller addiction can be very difficult, to healthcare professionals and patients

Table 4 Risk factors for diagnosis 'opioid use disorder'

	DSM-5 positive	DSM-5 negative	OR (95% CI)	Sig.
N (%)	54 (26.5%)	150 (73.5%)	N/A	N/A
Gender, male	23 (43.4%)	48 (32.7%)	1.18 (0.53 to 2.63)	0.69
Age* (mean [SD])	**55.47 (15.4)**	**64.06 (13.6)**	**0.96 (0.94 to 0.99)**	**0.003**
Duration of therapy >48 months	29 (56.9%)	82 (59.9%)	0.85 (0.40 to 1.78)	0.66
Depression	27 (55.1%)	53 (35.8%)	1.64 (0.76 to 3.53)	0.20
Basic compulsory education	24 (47.1%)	60 (42.3%)	1.27 (0.60 to 2.70)	0.53

Logistic regression analysis, n=170, df=5; n=absolute number of participants; (%)=percentage within variable DSM-5 - Score; Sig., Significance of OR.

alike. We do not know, whether the frequent selection of an item like 'failure to cut down or control opioid use' merely reflects the patients' frustration with chronic pain and his continuing need for opioid medication, therefore leading to an overdiagnosis of the disorder. Likewise 'reduction of social, occupational and recreational activities due to opioid use' may reflect the reality of chronic pain, rather than a direct result of problematic opioid use. Therefore, some of the mild cases might be misdiagnosed. However, items such as 'craving or a strong desire to use opioids' which could be suspected to be a result of insufficient pain therapy rather than OUD were shown to be linked to aberrant drug behaviour.[14]

In terms of validity, questions have been raised regarding the clinical and epidemiological effects of the lowered diagnostic thresholds of the new DSM-5 definition for OUD.[15 16]

Degenhardt *et al* found only fair to moderate agreement between ICD-10 and DSM-IV dependence diagnoses, and DSM-5 use disorder (mild, moderate or severe), but good agreement was found for moderate to severe use disorder.[17]

So it could be theorised that a diagnosis of mild OUD, at the most, points at a problematic pattern of opioid use and the need for preventive measures. In contrast, moderate to severe OUD with its good agreement with ICD-10 or DSM- IV dependence diagnoses might give a good indication of problematic use and the need for therapeutic measures.[18]

The rates for OUD we identified were within the range of other international studies. They ranged between 21%, 23% and 41.3% in the USA as well as 20.8% in Australia.[17 19 20] Comparable data from Germany does not exist yet. The correlation between young age and OUD was expected and is in line with prior findings from the USA.[21]

According to our findings, patients on LTOT for CNCP should be considered a risk group for OUD. Especially, the 9.3% with moderate to severe disorder may need additional specialist addiction therapy. The 'Guideline for prescribing opioids for chronic pain' delivers useful advice for increasing communication between providers and patients about the risks and benefits of opioid therapy for CNCP.[22]

We believe that the proportion of OUD during LTOT is dependent upon multiple physician and society related factors. Positive society related factors might have prevented the development of a 'US-style opioid epidemic' and the corresponding death toll in Germany. These factors may include compulsory, high-quality healthcare with adequate regulatory restrictions for opioids including a ban on direct to consumer marketing by the pharmaceutical industry. For the individual physician, it is important to know about patients' risk factors for opioid misuse and addiction enabling them to provide prevention, early diagnosis and adequate treatment of OUD.[18]

Additional studies focusing on larger population samples, including more patient criteria like daily opioid dose, are desirable in order to get a more detailed picture of OUD in Germany and Europe. Future interventions should focus on how to reduce proportions of OUD in chronic pain without impairing pain therapy itself.

CONCLUSION

More than one-fourth of patients in our sample were diagnosed with OUD and 9.3% showed moderate to severe disorder. In regard to the rather high rate of OUD, it is important to note that only moderate and severe cases (9.3%) agree well with ICD-10 or DSM-IV dependence diagnoses. OUD should be considered during follow-up in patients with CNCP.

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Data sharing statement All data used is available through the authors upon request.

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