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Patients' Perspectives on the Development of Prescription Opioid Use Disorder in Patients with Chronic Non-Cancer Pain

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Abstract
Introduction: In the past decade, prescription opioid use increased exponentially and concomitantly opioid use disorders (OUD) are becoming more common. Several risk factors for developing OUD have been identified, but little is known regarding the patients' perspective on developing a prescription OUD. ***Methods:*** We recruited 25 adults undergoing treatment for prescription OUD. In-depth, semi-structured interviews focussed on experiences with long-term opioid use, knowledge and attitudes regarding opioids, and access to opioids. A directed content analysis was conducted on the transcribed interviews using NVivo. ***Results:*** Participants showed that the development of an OUD is affected by various factors which could be grouped into three themes: (1) experiences driving initiation, (2) experiences driving continuation, and (3) experiences with prescription OUD. Besides the need for pain management, the dynamics of patient-provider communication, care coordination, provider vigilance, and environmental support all contributed to the way patients used their opioids. ***Conclusion:*** Patients' experiences illustrate that the first stage of the development of prescription OUD differs from the development of other substance addictions. Negative reinforcement might play a more prominent role in the early phase of prescription opioid use. Patients expressed a lack of guidance, both at the start of use and long-term use, easy access to new prescriptions and a lack of monitoring as main drivers of the development. Poorly controlled pain and subjective stress fuelled continuous opioid use.

Introduction

In the past decade, prescription opioid use has risen substantially worldwide [1–5]. In the Netherlands, the number of prescription opioid users nearly doubled from 4.1 to 7.5 per 100 inhabitants [3, 6], resulting in an increase in opioid misuse, opioid-related hospital admissions and mortality [3, 7, 8].

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Although there is no evidence that long-term opioid treatment is effective, opioids are still often prescribed for chronic non-malignant pain [9, 10]. In addition, long-term opioid use has several disadvantages, including risk of tolerance, with subsequent risks for dose escalation [11, 12].

Population surveys have shown approximately one out of ten people starting opioids for chronic pain develops an opioid use disorder (OUD) [13, 14]. OUD is characterised as a problematic pattern of use leading to problems or distress [15]. Demographic characteristics known to be associated with the risk of developing OUD are male sex, psychiatric comorbidities, chronic pain, history of benzodiazepine use, and previous addictive behaviour [16–19].

Most previous studies focussed on people using recreational drugs. Limited research has focussed on how people develop OUD on prescription drugs. The way patients experience both beneficial and side effects, as well as experiences of inadequately controlled pain, and the relief from emotional distress have been suggested to contribute to the development of an OUD [20]. However, the pathway to opioid dependence has not been studied in-depth.

Furthermore, most previous studies were performed in the USA. Difference in the organisation of health care may affect the development of OUD [21]. For example, one study found that the availability and price of heroin, as well as accessibility of prescription opioids in the UK, limit switching from prescription to illicit opioids, a very common pathway noted in USA settings [22].

In order to develop preventive measures and identify at-risk patients, a better understanding of the development of prescription OUD is necessary. The patients' perspective can provide valuable insights in this process and contributes to improved prescribing and monitoring of opioid use. This study aims to document patients' experiences on how they developed a prescription OUD.

Methods

Study Design

A qualitative study using in-depth, semi-structured interviews with patients under treatment for prescription OUD was conducted. The Medical Ethical Review Committee of Human Research Committee Radboudumc declared the research not subjective to the Dutch Medical Research Involving Human Subjects Act (WMO) (2020–7037). Subsequently, study procedures were reviewed and approved by the Utrecht University Institutional Review Board (division of Pharmacoepidemiology and Clinical Pharmacology (UPF 2018). All participants provided oral informed consent prior to participation. Afterwards, codes were assigned to all recordings, transcripts, and medical information, and identify-traceable information was removed. All recordings were deleted after completion of the data analysis. Participants did not receive compensation for participation.

Setting and Participants

In the Netherlands, opioids can only be prescribed by either a general practitioner (GP) or specialist care physician within their field of expertise. Guidelines for prescriptions of opioids limit the number of dosage units and require a regimen written in full. Guidelines for pharmacists require that they have an opioid administration. Opioids are fully reimbursed with respect that the first 385 euros spent on specialist and/or medication should be paid out-of-pocket.

Patients under treatment for a prescription OUD were recruited from two facilities: (1) Radboud University Medical Center (department of psychiatry) and (2) Novadic-Kentron (specialised addiction care facility), between November 2020 and July 2021. All patients were referred to these facilities that are specialised in the treatment of OUD. Eligibility criteria included being a Dutch speaking resident, age >18 years, previous use of opioids on prescription, having an OUD according to DSM-5 diagnosed during the intake procedure in addiction care.

Patients were informed about the study by their treating health care professional. If they were willing to participate and deemed stable enough to participate, patients were contacted by telephone by one researcher (L.D.) for further explanation of study procedures and to set an appointment for the 1-h interview. Due to COVID restrictions, all interviews were performed via telephone or video call. Patient recruitment continued until thematic data saturation was reached [23].

Data Collection

An interview guide based on the Prescription Drug Use Questionnaire was used to assess experiences with long-term opioid use, knowledge, and attitudes regarding opioids use and access to opioids [24]. Experiences with tapering were also examined but not discussed in this paper. The interview guide was iteratively refined after two interviews to ensure all relevant themes were addressed (online suppl. material; for all online suppl. material, see www.karger.com/doi/10.1159/000529926). Interviews were conducted by a trained interviewer (L.D.), who has a Masters in Epidemiology and followed multiple qualitative research courses including interview skills. In the first four interviews, a second researcher participated (V.D. – BSc.). The following patient characteristics were extracted from the patient's medical record: opioids used at clinical admission (name and dosage), comedication, and comorbidities.

Data Analysis

Audiotapes were transcribed verbatim and field notes were incorporated into the transcripts. Data were analysed using a directed content analysis using a pre-defined coding tree [25]. This coding tree was created prior to data collection, based on the interview guide and a review of literature for known risk factors of OUD development [7, 16, 17]. A new code was created when required. If required, codes were adjusted to reflect gained insights from the data or removed if not applicable. The final coding tree can be found in online supplementary material. The first four

interview transcripts were independently coded by two researchers (L.D., V.D.). Agreements were made on how to interpret, sort, summarise, and shorten quotes that supported a code. Afterwards, one researcher (L.D.) was the primary coder of the study. Codes were discussed with another member of the research team (E.K.). If disagreement occurred, the original transcripts were used for clarification.

One researcher (L.D.) conducted the initial categorisation of the codes. The generated concept categories and themes, supported by quotes, were evaluated regularly with members of the research team to ensure consistency of interpretation. NVivo, version 12 was used for data management and analysis. The findings were supported by illustrating quotes and reported according to the Consolidated Criteria for Reporting Qualitative Research (COREQ) [26].

Results

A total of 25 participants took part in the study, of which seventeen interviews were conducted via videocall (68%) and eight via telephone (32%). On average, patients were 53 years old, and 52% were female. All participants initially received opioids for chronic pain and 56% used opioids for at least 5 years. Most patients used oxycodone or a combination of opioids that included oxycodone (Table 1 and online suppl. Table 2).

We identified three major themes relevant for development of an OUD: (1) drivers of initiation, (2) maintenance drivers, and (3) experiences with prescription OUD. See Figure 1.

Theme 1: Drivers of Initiation

Internal Drivers

Participants reported starting opioid treatment because of wide variation of chronic pain complaints. Many participants described their pain as extremely debilitating. All participants perceived opioids as neutral or positive before start of treatment and were desperate for pain relief.

> "My nerve pain is so intense; I was happy with every suggestion. I was incredibly happy that there was a solution at all that made it liveable again, because it definitely wasn't before!" (P17, male, 40s).

Most participants noticed immediate pain relief when starting opioids. In the first instance, this improved their sleep quality and daily activities. Few participants experienced side effects at the start, but this did not deter them from further using opioids.

> "In principle, I could do everything again within boundaries. I went from unable to do anything to being able to participate in society" (P9, female, 50s).

Subsequently, some participants also stated that they realised the medication helped ease their emotional distress.

> "To be honest, I also felt mentally better due to the oxycodone. It was only meant for the pain, but to be fair I also used it for the nice feeling in the beginning." (P25, female, 40s).

External Drivers

Most participants received only information about the practical use of medication, but not regarding the potential risks of opioid use. A few described that their GP warned them to be careful but without further explanation.

> "It was just prescribed, without really informing me what it does to you. You are a patient with a lot of pain and you want that pain to go away so I guess you accept everything" (P8, male, 40s).

Most participants mentioned that they had multiple prescribers both in primary and secondary care. Often opioid treatment was started in secondary care and continued by the GP without additional consultation.

> "I first got the oxycodone from the GP and I was prescribed fentanyl by the emergency doctor and the GP continued this" (P1, female, 40s).

Furthermore, nearly all participants described that during treatment they could not remember any critical comment from physicians or pharmacists regarding their increasing opioid use. Participants stated that they trusted the expertise of their physicians.

> "It always comes back to that I trusted the expertise of the GP thinking he knows better than me. So I was kind of persuaded each time like: 'okay, it will be fine, let's take a few more pills or patches'" (P2, female, 30s).

Likewise, many participants stated that it was easy to obtain new opioids when required. To their own astonishment, many participants received prescriptions for large quantities of opioids.

> "I would get 100 pills of 5 mg, a 100 of 10 mg and a 100 of 30 mg and I would go home with a plastic bag saying: 'I've been to my dealer!' (sigh of disbelief) They would just give you a 3 months' supply!" (P22, male, 60s).

Theme 2: Drivers of Maintenance

Internal Drivers

The main reason for long-term opioid use was continuing or increasing pain complaints. However, a few participants also described using opioids for perceived beneficial effects on mental health such as anxiety or depression.

> "It was at first, in the first year maybe even the first 2 years for sure, very pain-driven and afterwards it became a mix as

Table 1. Participant characteristics

Participant characteristics (total *n* = 25)	
Gender, *n* (%)	
Female	13 (52)
Age, mean (SD)s	53 (±10)
Type of chronic pain indication to start opioid treatment, *n* (%)	
Chronic visceral pain	2 (8)
Chronic musculoskeletal pain	10 (40)
Chronic neuropathic pain	5 (20)
Chronic postsurgical and post-traumatic pain	6 (24)
Chronic widespread pain	2 (8)
Patient-identified duration of opioid use, *n* (%)	
<1 year	1 (4)
1–5 years	8 (32)
>5–10 years	5 (20)
>10 years	9 (36)
Unknown	2 (8)
Information collected at admittance in facility	
Average daily OME*	254±384 mg
Opioids used, *n* (%)	
Tramadol	1 (4)
Oxycodone	9 (36)
Fentanyl	5 (20)
Combinations	10 (40)
Other medication, *n* (%)	
Antidepressants	14 (56)
SSRI	6 (24)
TCA	8 (32)
Antipsychotics	5 (20)
Benzodiazepines	10 (40)
GABA (e.g., pregabalin)	8 (32)
Other painkillers (e.g., ibuprofen, paracetamol)	10 (40)

*Oral morphine equivalent at intake of addiction care facility.

you're a little bit depressed, kind of aimless, you're rejected (due to the impact of chronic pain on their daily life)." (P13, male, 50s).

Nearly, all participants noticed that over time their initial starting dose was not sufficient to suppress their pain, resulting in requests for increased dosages. This cycle of reduced efficacy accelerated over time, with most participants noticing insufficient pain control within half a year of use.

"But you still keep using that oxycontin and oxynorm without a thought, … Because I didn't recover and you keep trying and then you start using what you got prescribed more and more to see if this will be that little push that you need to start healing." (P10, male, 50s).

Over time participants realised they could no longer function without their medication and had become dependent. Not using their opioids was followed by severe withdrawal symptoms and recurring pain. Taking their opioids suppressed these symptoms leading to a cycle of increasing use.

"Yes, I could notice it myself each time as I took a pill, for example, I took one every 4 h and when I did not take it on time then I would start to feel very bad! Incredibly unhappy, I got palpitations and I started to shake and as soon as I took the oxycodone I was fine again" (P14, male, 60s).

Ultimately, some participants stated that they had to continuously use opioids and developed a craving for either pain relief or mental numbing effects. Participants described constantly wanting and trying to get more opioids. Some even stated that they felt "like addicts."

"I also felt like a junky, a drug user, because I needed it all the time. The feeling is hard to describe, but you're shaking a lot and you are constantly thinking about oxycodone." (P8, male, 40s).

Several participants expressed that they tried to request more prescriptions as well as trying to pick up their

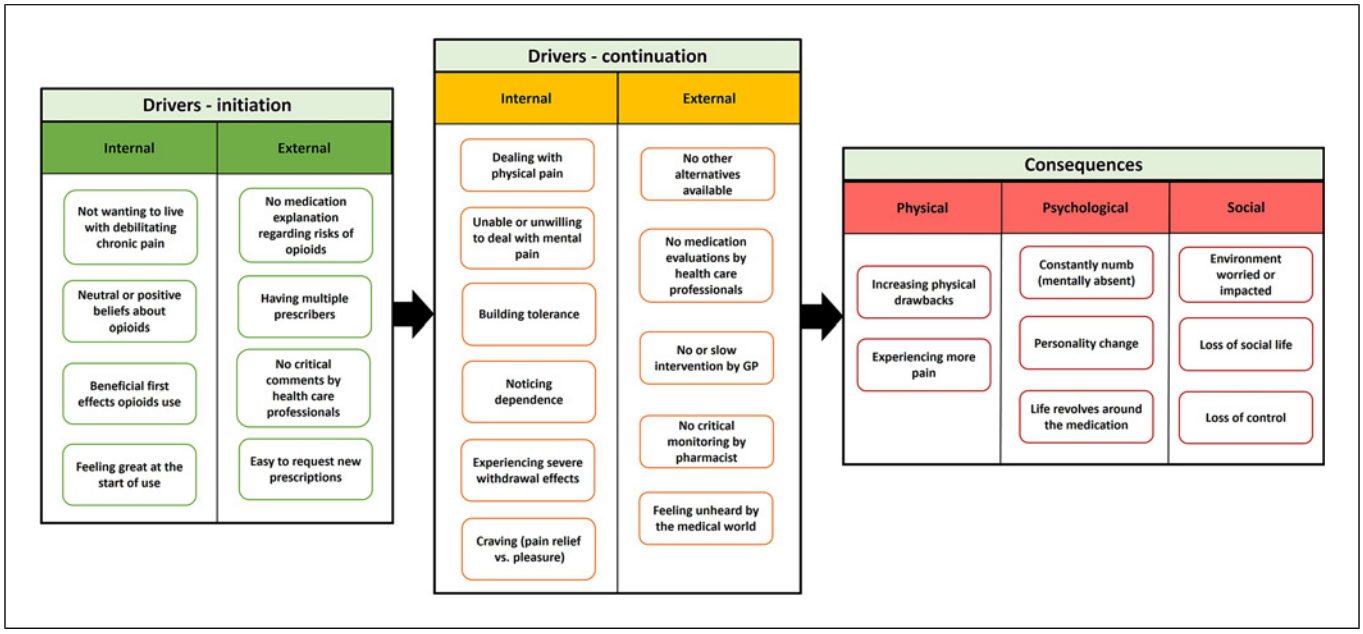

Fig. 1. Development of a prescription opioid use disorder.

prescriptions earlier. Furthermore, some participants were so anxious about running out of opioids that they started stockpiling.

> "I was afraid that if I said 'Listen, I've used way too much this week and now I'm running short for the weekend,' 'Sure, you shouldn't have done that' (pharmacy) and then you wouldn't get anything. . . . Thus, that's why I would make an excuse like the pharmacy didn't deliver. Thus I would order more as I was too afraid that I would not get anything." (P11, male, 50s).

In addition, some participants searched for different ways to obtain opioids such as looking for other potential prescribers, i.e., hospitals settings or emergency care facilities, or some even scoured the internet for additional medication.

> "I looked it up on the internet and got it illegally and that way I got more and more permanent addresses. I could get unlimited oxycodone supply and I never was a day without." (P25, female, 40s).

External Drivers

Many participants stated that they had no suitable alternative for opioids. Therefore, participants felt that they had no other option but to continue use to relieve their pain.

> "And they all said (HCP): 'There is nothing we can do about that! You'll end up in a wheelchair.' So, there was nothing to be done, but swallowing pills. So, that's what I did." (P7, male, 60s).

Most participants rarely received a critical comment from their health care professional regarding their opioid use.

> "I've never been asked that in all the ten or 9 years I've been using it. . . . 'Gosh, let's take some time to review all your medication to see where you should cut back a bit.' Never!" (P10, male, 50s).

Participants described that they seldom had a medication evaluation, and more than half the participants never obtained a warning from their pharmacist during long-term use. Sometimes they received a comment about trying to pick up prescriptions earlier than intended and the pharmacist consulted the GP. However, this rarely resulted in an intervention other than a delayed opioid prescription.

> "Then the GP had to write another prescription and the pharmacist has said that she often communicated with the GP to ask: 'Is this going well or can we do it differently?'. In that area the pharmacy did more for me than the GP." (P2, female, 30s).

Often a change in attitude was perceived when participants either reached the maximum dose or switched GP's, with health care professionals becoming more reluctant to prescribe more opioids. However, in most cases, participants noted that their GP also did not know how to further treat them.

> "The GP didn't know what to do anymore either, at a certain point he had prescribed me everything, partly out of pity, what he could offer." (P15, female, 50s).

Once the escalated use had reached a limit the attitude of their GP and pharmacist seemed to rapidly change negatively towards opioid prescriptions. This resulted in participants feeling like they had nowhere to turn as they were no longer able to get more opioids, yet there was no other alternative. A few participants underlined that they felt unheard and their remarks about escalating use where not taken seriously when they reported it.

> "Despite the fact that I raised the alarm often and made statements that I did no longer wanted to use in this manner and that I felt incredibly bad, it was often ignored. There was simply no response." (angry, frustrated) (P2, female, 30s).

Theme 3: Experiences with an OUD

Physical Consequences

Although initially increasing quality of life, many participants described that over time they noticed more drawbacks of long-term use such as feeling drowsy, tooth decay, severe obstipation, and a disturbed day-night rhythm. Few described that the overall constant sedation resulted in muscle atrophy, unnoticed fractures and infections, and memory loss with participants losing days up to months.

> "Everything, your immunity goes to hell, you don't sleep therefore your body cannot recover, you want to do things, but you can't. Taking out the garbage was similar to running a marathon! Everything was screwed up!" (P7, male, 60s).

Few participants also described increased sensitivity of pain stimuli (hyperalgesia), resulting in them requiring more opioids to suppress their pain.

> "I think that my sense of pain at that time was also amplified at some point by the oxycodone." (P15, female, 50s).

Psychological Consequences

Many participants described a feeling of being out of touch with their environment under the influence of opioids. Terms like feeling numb, under a blanket, or like a zombie were often used. This also impacted their social environment.

> "Of course, it was not great for my daughter and husband. I mean I would sit there on the couch (physically) but I was not really there (mentally). I was useless for the people around me." (P15, female, 50s).

Quite a few participants described how they gradually became preoccupied by thoughts of their next dose and fears of running out. Activities were planned around their opioid use instead of the initial use to perform activities.

> "In the end I had no life anymore. Everything was based on those tablets and that also applied to my wife and children. If we went to a party then it had to be calculated correctly with those tablets, otherwise I wouldn't join them." (P14, male, 60s).

Most of these participants noticed that their personality changed. Participants experienced mood swings, apathy, and irritability, especially when their opioid use was questioned, or their dose had worn off. Some participants developed suicidal ideation.

> "I can talk to everyone when I've taken them, but the moment they wear off and I come to the part that I'm missing them then I don't want anybody to come near me!" (P6, male, 60s).

Social Consequences

Participants often received comments on their opioid use from their environment. While some experienced understanding, most received negative responses.

> "I kept using. I have pictures (from that time) that my son took. He would say: 'Dad, look, this is what I see every day!'" (shows picture of a person knocked out, pale, eyes rolled back and open mouth) (P14, male, 60s).

Eventually, participants stated that the adverse effects especially the cognitive and personality changes resulted in loss of work, friendships, relationships, and for a few even lead to social isolation.

> "Over the years I have lost everything: my girlfriend, job, my friends, hobbies, passions, sports. Last year I also lost my house. So yeah, the past 5 years I've gone through extreme hell, and I'm keep getting more physical complications and I don't know when it will end but it just keeps going, unfortunately." (P8, male, 40s).

Discussion

From a patients' perspective, the development of prescription OUD starts with the lack of adequate information at the start of treatment. In line with previous research, we found that chronic pain profoundly affected patients' life leading to a desperate longing for pain relief combined with receiving inadequate information regarding risks of long-term treatment. The initially beneficial effects of opioids (e.g., increased mobility due to pain relief) subsequently drive continued use [27]. Additionally, patients described initial easy access to repeat prescriptions sometimes in large quantities without critical questioning by their health care providers. Hence, without reason for concern, patients were more likely to naively increase their dose according to their chronic pain complaints leading to unchecked escalating opioid use.

Although prescription OUD is classified as substance use disorder (SUD) according to the DSM-5 [15], when it concerns prescription opioid initiation it does not always seem to follow the typical pathway of addiction like other

SUDs such as alcohol and other drugs [28]. According to the addiction model of Volkow and Koob, there are three stages for developing addiction: binge intoxication, withdrawal and negative effect, and preoccupation and anticipation [29]. However, only few patients in our study described feelings that could be classified as blissful (euphoric) or opioid binging at the start of treatment. Instead, using opioids provided a relief of a negative effect (chronic pain and in a later stage relief of withdrawal symptoms) rather than providing a positive effect (high). This distinction is important when trying to recognise patients at risk for initial escalation as among patients with (chronic) pain negative reinforcement mechanisms (compulsivity) might be more prominent than positive reinforcement mechanisms (impulsivity) in driving opioid use.

The ineffective pain control, due to increasing pain complaints and developing tolerance to current dosages, as well as experiencing alleviated emotional distress when using opioids reinforced continued use. This first stage of the development of OUD as described by patients seems consistent with previous research into patient experiences with OUD [19, 20]. In the later stages of the development of OUD patients described the well-known cycle of dependence: heavy use progresses to a point where not using opioids was followed by severe withdrawal symptoms and recurring pain. This results in patients feeling unable to function without medication. This negative reinforcement cycle is well documented in patients with other substance use disorders and can be considered a major driver in progressing to the final stages of developing a prescription OUD [29].

Compared to development of SUDs there is another major difference, namely, the perceived role that health care providers play in the prescription OUD development. While studies performed in the USA often describe that individuals starting prescription opioid treatment switch to illegal opioids to support their needs [20, 21], this was not apparent in our population. Probably as patients stated that costs of illegal opioids compared to the covered legal medication prevented them from switching. Patients indicated that they could easily get more opioids when desired by requesting new prescriptions as they rarely received critical comments regarding their increasing and long-term use.

Furthermore, patients often received prescriptions from several prescribers in primary and secondary care. Additional opioid prescriptions from secondary care were often continued by the GP without evaluation. This may be explained by the fact that although health care professionals are often aware of the adverse effects of opioids, they remained concerned that deciding not to prescribe would lead to unnecessary suffering [30, 31] or a loss of their patient-provider relationship. Yet, once patients describe being completely dependent the attitude of health care providers seemed to change rapidly. Prescribers did not want to further escalate prescribing and put patients on a fixed ration of opioids, but they did not help them to deescalate their opioid use. Patients described losing trust in their prescriber as they felt they were partly responsible for their developed dependence. So, without an alternative and nowhere to turn to they felt forced to keep using.

Implications

Our findings indicate that patients require a thorough explanation regarding the risks of opioids at the start of treatment as this increases patient involvement regarding their opioid intake. Similar to a recent French study the majority of opioid users reported that no health care professional had informed them of the risks [32]. This explanation should include risk of dependence, withdrawal, and developing an OUD, expectations regarding long-term use and when to alert their health care professional. Our results also emphasize the importance of repeated counselling as many patients experienced cognitive impairment when using opioids.

Given that most patients in our sample indicated that poorly controlled pain was the main driver of misuse, it seems critical that prescribers set realistic expectations for pain management, stress the importance of non-pharmacologic treatments, and regularly evaluate effectiveness and appropriateness of opioid therapy. Additionally, in treatment health care professionals should also focus on other outcomes of adequate pain treatment (e.g., socialisation, emotional improvement, physical activities). Also, in light of the finding that some patients may be desperate for pain relief, we like to stress that prescribers set a maximum prescription term for manageable problems (i.e., pain after surgery or accident). This could be in the form of a therapeutic contract at initiation of treatment. Furthermore, we recommend clear care communication between health care providers especially between the GP and pharmacist who both may signal escalating use [33].

Finally, it is important to note that patients with chronic non-malignant pain generally do not experience the classic binge and intoxication phase (impulsivity), which is often heavily focussed on in regular addiction treatment programmes. Thus, we

recommend treatment of prescription OUD should focus on reducing the negative reinforcement cycle (compulsivity) by providing effective chronic pain coping strategies as well as supporting the withdrawal process. Further research should investigate the role of health care providers can play in preventing the development a prescription OUD.

Strengths and Limitations

To our knowledge, this is the first study to investigate the development of a prescription OUD in chronic non-malignant pain patients. Furthermore, the qualitative research design provided in-depth, rich data on the patients' perspectives and allowed for follow-up questions revealing new information, which quantitative research cannot answer.

A few limitations should be noted. Recall bias should be taken into account as participants had to remember what they thought at the start of opioid treatment and what they thought and felt during periods using high dosages of opioids. Some patients stated experiencing memory loss due to heavy use and had a companion present during the interviews to help them along if they required assistance. However, we believe that this interference was minimal as their stories aligned with those interviewed without companion.

Furthermore, we mostly interviewed patients who completed a specific opioid treatment programme or were in the further stages of treatment rather than in the beginning stages. Thus, our results describe a cohort of chronic pain patients seeking treatment for their prescription OUD. Future work should investigate whether patients not in treatment at such specialized facilities might have other views.

Finally, most literature that focusses on the development of an OUD focusses on factors on patient level, such as genetics, personality traits, and psychiatric morbidity [14, 16, 17]. Yet, none of the patients specifically described this as being an influential factor in their development process. This might be due to the fact that we talked to patients themselves who are more likely to first point outwards rather than inwards.

In conclusion, our study showed that the first stages of a prescription OUD differ from SUD development. The initiation is driven by insufficient pain control rather than a positive impulse. Subsequently, prescription OUD follows the familiar cycles of dependence and withdrawal where opioids are used to avoid negative effects eventually driving into the final stages of a use disorder. A thorough understanding of the development of prescription OUD is essential to design appropriate prevention strategies. Special attention should be paid to opioid risk communication and evaluation with the patient and the potential role of the health care provider.

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Statement of Ethics

The research proposal was deemed exempt from the Dutch Medical Research Involving Human Subjects Act (WMO) by the Medical Ethical Review Committee Human Research Committee Radboudumc, approval number (2020-7037). The study protocol was reviewed and approved by Utrecht University Institutional Review Board (Division of Pharmacoepidemiology and Clinical Pharmacology), approval number (UPF 2018). All participants provided recorded oral informed consent prior to participation. Participants received patient information letter and informed consent letter beforehand. Due to COVID restrictions, the choice for oral informed consent was approved by the Utrecht University Institutional Review Board (Division of Pharmacoepidemiology and Clinical Pharmacology), approval number (UPF 2018).

Conflict of Interest Statement

All authors declare no conflict of interest.

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Author Contributions

L.D., E.S., A.S., and M.B.: conceived the project, developed the methodology, and planned the study. L.D. and E.S. were involved in the formal analysis of the data. All authors were involved in the investigation of the further themes, discussion of this study, and reviewed and edited the manuscript. K.D. and H.B. were involved in data collection. E.S., A.S., and M.B. supervised the project. L.D. wrote the original draft.

Data Availability Statement

Due to the confidentiality agreements and the sensitivity of the topic for research participants, supporting data are not publicly available. Data are, however, available upon reasonable request. Further enquiries can be directed to the corresponding author (M.B.). It should be noted that raw data are only available in Dutch.

References

1 Verhamme KMC, Bohnen AM. Are we facing an opioid crisis in Europe? Lancet Public Health. 2019;4(10):e483–4,
2 Hamunen K, Paakkari P, Kalso E. Trends in opioid consumption in the Nordic countries 2002–2006. Eur J Pain. 2009;13(9):954–62.
3 Kalkman GA, Kramers C, van Dongen RT, van den Brink W, Schellekens A. Trends in use and misuse of opioids in The Netherlands: a retrospective, multi-source database study. Lancet Public Health. 2019;4(10):e498–505.
4 van Amsterdam J, Pierce M, van den Brink W. Is Europe facing an emerging opioid crisis comparable to the US? Ther Drug Monit. 2021;43(1):42–51.
5 Celentano D. The worldwide opioid pandemic: epidemiologic perspectives. Epidemiol Rev. 2020;42(1):1–3.
6 Weesie YM, Hek K, Schermer TRJ, Schellevis FG, Leufkens HGM, Rook EJ, et al. Use of opioids increases with age in older adults: an observational study (2005–2017). Front Pharmacol. 2020;11:648.
7 Bedene A, Lijfering WM, Niesters M, van Velzen M, Rosendaal FR, Bouvy ML, et al. Opioid prescription patterns and risk factors associated with opioid use in The Netherlands. JAMA Netw Open. 2019;2(8):e1910223.
8 Bedene A, van Dorp ELA, Faquih T, Cannegieter SC, Mook-Kanamori DO, Niesters M, et al. Causes and consequences of the opioid epidemic in The Netherlands: a population-based cohort study. Sci Rep. 2020;10(1):15309,
9 Kissin I. Long-term opioid treatment of chronic nonmalignant pain: unproven efficacy and neglected safety? J Pain Res. 2013;6:513–29.
10 Von Korff M, Kolodny A, Deyo RA, Chou R. Long-term opioid therapy reconsidered. Philadelphia: American College of Physicians; 2011.
11 Chou R, Deyo R, Devine B, Hansen R, Sullivan S, Jarvik JG, et al. The effectiveness and risks of long-term opioid treatment of chronic pain. Evid Rep Technol Assess. 2014(218):1–219,
12 Volkow N, Benveniste H, McLellan AT. Use and misuse of opioids in chronic pain. Annu Rev Med. 2018;69:451–65.
13 Els C, Lappi VG, Kunyk D, Sharma S, Sonnenberg B, Hagtvedt R, et al. Adverse events associated with medium-and long-term use of opioids for chronic non-cancer pain: an overview of Cochrane Reviews. Cochrane Database Syst Rev. 2017;10(10):CD012509.
14 Vowles KE, McEntee ML, Julnes PS, Frohe T, Ney JP, van der Goes DN. Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis. Pain. 2015;156(4):569–76.
15 Association AP. Diagnostic and statistical manual of mental disorders (DSM-5®). Washington (DC): American Psychiatric Pub; 2013.
16 Cochran BN, Flentje A, Heck NC, Van Den Bos J, Perlman D, Torres J, et al. Factors predicting development of opioid use disorders among individuals who receive an initial opioid prescription: mathematical modeling using a database of commercially-insured individuals. Drug Alcohol Depend. 2014;138:202–8.
17 Edlund MJ, Martin BC, Fan M-Y, Devries A, Braden JB, Sullivan MD. Risks for opioid abuse and dependence among recipients of chronic opioid therapy: results from the TROUP study. Drug Alcohol Depend. 2010;112(1–2):90–8.
18 Strang J, Volkow ND, Degenhardt L, Hickman M, Johnson K, Koob GF, et al. Opioid use disorder. Nat Rev Dis Primers. 2020;6(1):3,
19 Weiss RD, Potter JS, Griffin ML, McHugh RK, Haller D, Jacobs P, et al. Reasons for opioid use among patients with dependence on prescription opioids: the role of chronic pain. J Subst Abuse Treat. 2014;47(2):140–5,
20 Stumbo SP, Yarborough BJH, McCarty D, Weisner C, Green CA. Patient-reported pathways to opioid use disorders and pain-related barriers to treatment engagement. J Subst Abuse Treat. 2017;73:47–54.
21 Cicero TJ, Ellis MS. The prescription opioid epidemic: a review of qualitative studies on the progression from initial use to abuse. Dialogues Clin Neurosci. 2017;19(3):259–69.
22 Weisberg DF, Becker WC, Fiellin DA, Stannard C. Prescription opioid misuse in the United States and the United Kingdom: cautionary lessons. Int J Drug Pol. 2014;25(6):1124–30.
23 Guest G, Bunce A, Johnson L. How many interviews are enough? An experiment with data saturation and variability. Field methods. 2006;18(1):59–82.
24 Compton PA, Wu SM, Schieffer B, Pham Q, Naliboff BD. Introduction of a self-report version of the prescription drug use questionnaire and relationship to medication agreement noncompliance. J Pain Symptom Manage. 2008;36(4):383–95,
25 Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. Qual Health Res. 2005;15(9):1277–88.
26 Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care. 2007;19(6):349–57.
27 Nichols VP, Toye F, Eldabe S, Sandhu HK, Underwood M, Seers K. Experiences of people taking opioid medication for chronic non-malignant pain: a qualitative evidence synthesis using meta-ethnography. BMJ open. 2020;10(2):e032988.
28 Beurmanjer H, Asperslag EM, Oliemeulen L, Goudriaan AE, De Jong CAJ, Schellekens ASA, et al. A qualitative approach in understanding illness perception and treatment needs in patients with gamma hydroxybutyrate use disorder. Eur Addict Res. 2019;25(5):248–55.
29 Volkow ND, Koob GF, McLellan AT. Neurobiologic advances from the brain disease model of addiction. N Engl J Med. 2016;374(4):363–71.
30 Toye F, Seers K, Tierney S, Barker KL. A qualitative evidence synthesis to explore healthcare professionals' experience of prescribing opioids to adults with chronic non-malignant pain. BMC Fam Pract. 2017;18(1):94,
31 McCrorie C, Closs SJ, House A, Petty D, Ziegler L, Glidewell L, et al. Understanding long-term opioid prescribing for non-cancer pain in primary care: a qualitative study. BMC Fam Pract. 2015;16(1):121,
32 Lavergne J, Debin M, Blanchon T, Colizza V, Dassieu L, Gimenez L, et al. Perceived risk of opioid use disorder secondary to opioid analgesic medication use by the general population in France. Eur J Pain. 2022;26(3):729–39.
33 Gregory T, Gregory L. The role of pharmacists in safe opioid dispensing. J Pharm Pract. 2020;33(6):856–62.