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Non-Cancerous Chronic Pain as a Risk Factor of Opioid Use Disorder (OUD): A Systematic Review

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Abstract

Non-Cancerous Chronic Pain (NCCP) is a common disease that imposes significant health costs to the population and impacts the health of a significant percentage of people. It is a comprehensive review article about the relationship between Non-cancerous chronic pain and the risk of developing Opioid Use Disorder (OUD). An extensive search of various databases was made to identify the corresponding papers that were published in 2005-2023 in English language. Findings indicate that Non-cancerous chronic pain is strongly connected with opioid use disorder. People who use opioids to manage their chronic pain are also at risk of developing opioid use disorder. It was observed that this heightened risk had been precipitated by factors such as the continued use of opioids, rising doses of opioids, comorbid psychiatric disorders and even the underlying disorder. Additionally, opioids prescribed to manage acute pain risk developing chronic pain, which is another risk factor that promotes opioid abuse. The review highlights that a comprehensive approach to the management of chronic pain involves the incorporation of non-opioid intervention, responsible prescribing guidelines, and patient education. Non-opioid pain management needs to be combined with non-pharmacological treatment options including physical therapy and cognitive-behavioral therapy. Continuous monitoring, comprehensive management approaches incorporating both physical and psychological therapy, and screening of comorbidity are all requisite components of an effective management of pain. Further research and policy interventions are needed to build knowledge, enhance addiction treatment resources, and improve access to non-pharmacological approaches to treating pain.

Keywords*: non-cancerous chronic pain, opioid misuse, opioid use disorder, pain relief*

Picture, a life filled with unrelenting agony, where even the simplest delights are taken away by tenacious, debilitating pain. This miserable reality is experienced by millions globally who suffer from chronic pain. In search of respite, many turn to powerful opioid medications, oblivious of the traitorous path they may unintentionally walk (Speed et al., 2018). Chronic pain is a profoundly debilitating condition affecting a substantial portion of the worldwide population ("Practice Guidelines for Chronic Pain Management," 2010).

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As Keefe et al. (2004) revealed in their study chronic pain is described by persistent or repeated pain lasting for three months or more, often caused by various underlying medical conditions or injuries. To cope with chronic pain, opioid pain relievers are frequently prescribed due to their powerful pain-relieving properties (Turris, 2008). However, the prolong use of opioids raises fears about the possible development of misuse and addiction (MacLean et al., 2021). Robinson et al. (2018) also indicated in their study that chronic pain conditions have become progressively prevalent, and as a result, there has been a parallel rise in both the utilization and misuse of opioids.

In this systematic review, we will only be considering non-cancerous chronic pain. Non-cancerous chronic pain refers to persistent pain that continues for an extended timeframe (typically three months or longer) and is unrelated to cancer or its treatment (Morasco et al., 2011). It is also associated with an array of conditions and may affect a wide spectrum of body, including

muscles, nerves or organs (Cooke et al., 2019). Non-cancerous chronic pain can have another reason, such as injuries, inflammation, nerve damage or other chronic diseases (Ras, 2020). Chronic pain that is not cancerous can be severe, and affect physical activity of an individual, mood, and overall life experience (Rauf et al., 2013). Non-cancer chronic pain is generally treated using a multimodal approach that may or may not include pharmacological therapy, physical therapy, psychological support, lifestyle modifications and complementary therapies (Cáceres-Matos et al., 2020). Opioid drugs are sometimes used to treat severe chronic non-cancer pain, but treatment with such drugs should be closely supervised due to the potential risk of misuse, addiction, and other adverse effects of long-term opioid treatment (MacLean et al., 2021). Though the relationship between chronic pain and the abuse and dependence of opioids has already been studied, the number of research studies directly related to Non-cancerous chronic pain may be limited (Nadeau et al., 2021). Further, Non-cancerous chronic pain is a unique subset of the general chronic pain population. Chronic pain associated with cancer and the etiology, nature as well as treatment of that type of pain vary with non-cancerous chronic pain (Goesling et al., 2018). When narrowing the focus on Non-cancerous chronic pain, we would learn more specific and relatable information regarding the specific form of pain and the abuse and addiction of opioids.

Opioid abuse is the use of prescription opioids improperly or in non-therapeutic ways or the use of opioid medications in a manner that is not in line with the instructions given by the prescriber (Robinson et al., 2018). It is associated with overdosing on an opioid, taking opioids without any pain considerations, and purchasing opioids illegally (Ledger, 2020). Currently, opioid use disorder, or opioid addiction, is a chronic health condition marked by continued and compulsive opioid-seeking behaviors, the inability to control opioid use, and continued use of opioids in spite of their adverse effects (Manchikanti et al., 2004). According to a study conducted by Turris (2008), opioid misuse can be very dangerous to the overall health and wellbeing of an individual. It may cause different adverse effects, such as development of opioid use disorder, overdose, physical dependence, tolerance, withdrawal symptoms, and impaired cognitive and motor performance, social and legal problems. Opioid abuse in the long run will lead to a downward spiral of increasing drug seeking behavior with negative consequences (Malta et al., 2019).

The methodological tool that can be utilized in order to appraise the literature, and trends that are available and synthesize the evidence that has been acquired on a specific research question is the systematic review (Moher, 2009). In this systematic review, we would seek to investigate the possible role of chronic pain as an opioid misuse and addiction risk factor. The implications of the findings of this systematic review will have significant clinical practice and policy development outcomes. The understanding of chronic pain as a risk factor in the development of opioid use disorder and addiction may assist healthcare providers to better evaluate and address the risks that opioid therapy can pose in this population. The review will also inform the development and efficacy of intervention and preventive strategies to minimize opioid use disorder among chronic pain patients.

Overall, this systematic review will provide a multidimensional perspective on the association between chronic pain and the risk of opioid misuse and addiction. The current review will contribute to the existing body of work and will influence future research and practice in this field of chronic pain management on the basis of the synthesis of the existing evidence we have.

Method

Research Question

The following investigating question is part of this systematic review: Is non-cancerous chronic pain a predictor of opioid use disorder? (OUD)?

Retrieval plan

Data Basis

A thorough search was performed using multiple databases, including Scopus, MEDLINE, Web of Science, PsycINFO, Google Scholar, Science Direct, PubMed, and OvidSP. The search was limited to studies published in the English language. Additionally, reference compilations of pertinent academic papers and systematic literature reviews were thoroughly examined to identify any additional studies that fulfilled the inclusion criteria.

Retrieval Terms

"Non-cancerous chronic pain" OR "Chronic pain" OR "Persistent pain, Non-cancer pain OR Long-term pain" AND "Opioid use disorder" OR "Substance use disorder" OR "Prescription opioid misuse" OR "Opioid abuse" OR "Opioid dependence" OR "Opioid misuse predictors" OR "Risk factors for opioid use disorder" OR "Chronic pain and opioid misuse" OR "Chronic pain and substance use disorder" OR "Chronic pain and prescription opioid abuse" "Persistent pain and opioid use disorder"

Inclusion Criteria

The following are the points for study inclusion criteria:

- Studies investigating the correlation between non-cancerous chronic pain and opioid use disorder.
- Studies that assess non-cancerous chronic pain as a predictor or factor contributing to the risk of developing opioid use disorder.
- Studies involving human participants of any age or sex.

- Studies published in English (or provide English translations).
- Studies from 2005 to 2023
- All types of study designs (e.g., observational studies, experimental studies, qualitative studies, case reports, and case studies) are eligible for inclusion.

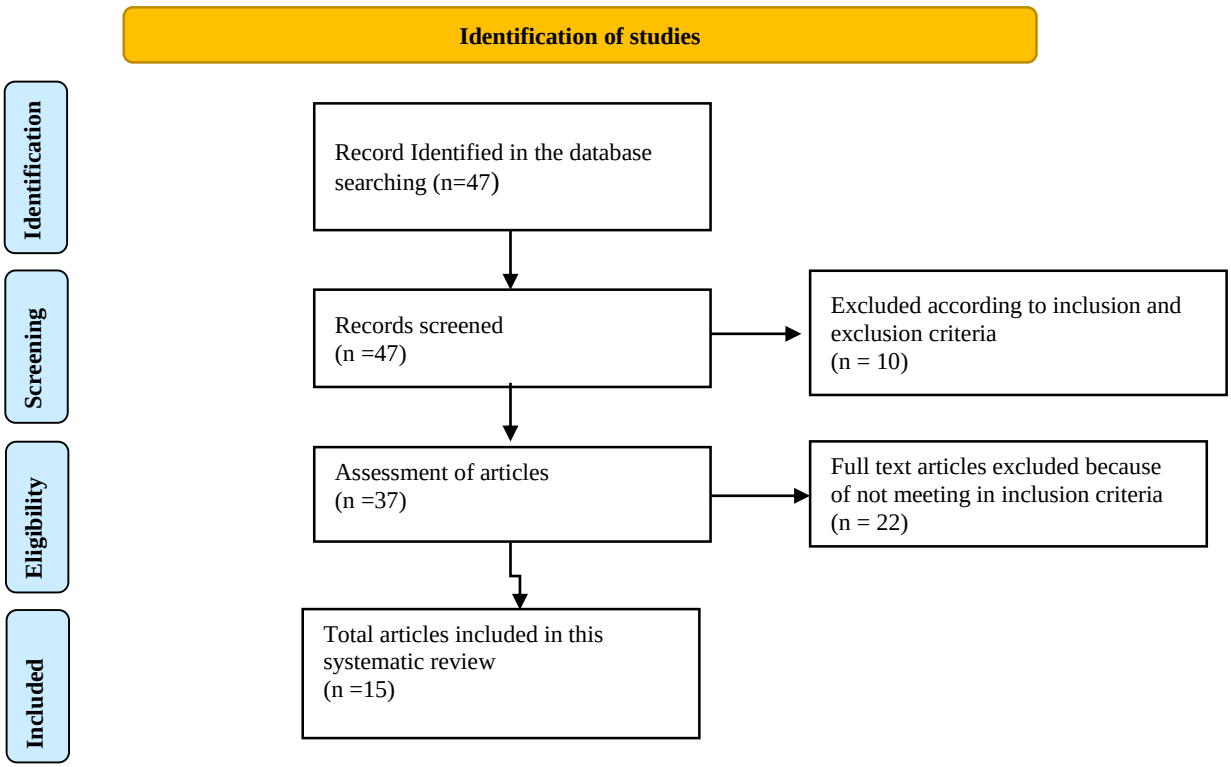
Exclusion Criteria

The following are points for study exclusion criteria:

- Studies conducted solely on animals were excluded, as the focus of your review is on human participants.
- Reviews, Editorials, and Opinion Pieces
- Studies focused solely on cancer-related pain
- Acute Pain Studies as this systematic review's focus is on non-cancerous chronic pain.
- Non-English Studies without Translations:
- Studies published prior to 2005 or subsequent to 2023

Figure 1

PRISMA Flow Diagram of Study Selection



Method for selecting relevant studies

Two autonomous reviewers executed the first-stage screening of titles and abstracts identified through the search strategy. Full-text publications of studies with potential relevance were then obtained and scrutinized for eligibility based on the criteria used to determine inclusion and exclusion. Any incongruities between the reviewers were resolved through mutual.

Data Extraction

A standardized data recording template/table was developed and utilized to extract pertinent information from the selected

studies. The extracted information included various features, including study characteristics (authors, year of publication, sample size, study design and method, and geographical location), participant characteristics (demographics, chronic pain diagnosis, opioid use disorder diagnosis, and comorbidities), assessment measures and criteria employed to evaluate non-cancerous chronic pain and OUD, outcome measures related to non-cancerous chronic pain as a risk factor of an opioid use disorder (OUD), and reported results such as effect sizes, odds ratios, relative risks, and relevant statistical measures. This comprehensive data extraction process enabled the acquisition of essential details for subsequent analysis and synthesis of the included studies. The systematic review specifically focused on qualitative studies. The rationale behind focusing solely on qualitative studies in this systematic review was to delve deeply into the subjective experiences, perceptions, and emotions concerning non-cancerous chronic pain and its link to Opioid Use Disorder (OUD). Greater insight into the intricate relationship between these elements would have been possible with the qualitative research alternative due to the fact that it provided us with much more information regarding the individual attitudes and experiences of the affected individuals.

Table 1

Features of the Included Studies

Sr. No.	Title	Study Reference	Country	Study Framework	Population Profile
1.	Relationship of Opioid Use and Dosage Levels to Fractures in Older Chronic Pain Patients	(Saunders e t al., 2010)	USA	Epidemiological	Age: 60 years and older N=2,341
2.	Long-term efficacy and safety of combined prolonged-release oxycodone and naloxone in the management of non-cancer chronic pain	(Sandner-Kiesling et al., 2010)	Germany	RCT	Age: 18 - 60 years N = 379
3.	Cross Validation of the Current Opioid Misuse Measure (COMM) to Monitor Chronic Pain Patients on Opioid Therapy	(Bulter, et al., 2010)	USA	Experimental	Age: 18 - 87 years N = 226
4.	Long-Term Chronic Opioid Therapy Discontinuation Rates from the TROUP Study	Martin at al., 2011)	USA	Experimental	Age: 20 - 60 years N = 6,848
5.	Compliance with Opioid Treatment Guidelines for Chronic Non-Cancer Pain (CNCP) in Primary Care at a Veterans Affairs Medical Center (VAMC	(Sekhon et al., 2013)	USA	Retrospective	Age: 18 and 87 years N = = 797
6.	Buprenorphine – an attractive opioid with underutilized potential in treatment of chronic pain	(Khanna, & Pillarisetti, 2015)	USA	RCT	Age: 20 - 50 years N = 32
7.	Psychiatric disorders among patients seeking treatment for co-occurring chronic pain and opioid use disorder	(Barry et al., 2016)	USA	Experimental	Age: 18 - 60 years N = 170
8.	Higher Prescription Opioid Dose is associated with Worse Patient-Reported Pain Outcomes and More Health Care Utilization	(Morasco et al., 2017)	Portland	RCT	Age: younger than 18 years N = 517
9.	Risk of opioid misuse in chronic non-cancer pain in primary care patients - a cross sectional study	(Just et al., 2018)	Germany	Cross sectional	Age: 18 - 60 years N = 91
10.	Opioid Medication Use Among Chronic Non-Cancer Pain Patients Assessed with a Modified Drug Effects Questionnaire and the Association with Opioid Use Disorder'	Boscarino, et al., 2019)	USA	Cross-sectional	Age: 18 - 45 years N = 200
11.	Opioid use disorder in chronic noncancer pain in Germany: a cross sectional study	(Just et al., 2019)	German	Cross-sectional	Age: 18 - 60 years N = 204
12.	Chronic pain diagnoses and opioid dispensings among insured individuals with serious mental illness	(Owen-Smith et al., 2020)	USA	Cross-sectional	Age: 18 - 70years N = 304

13.	Beneficial Effects of Opioid Rotation to Buprenorphine/Naloxone on Opioid Misuse, Craving, Mental Health, and Pain Control in Chronic Non-Cancer Pain Patients with Opioid Use Disorder	(Schellekens et al., 2021)	Netherlands	Prospective, Observational	Age: 18 - 65 years N = 43
14.	Psychiatric comorbidity and order of condition onset among patients seeking treatment for chronic pain and opioid use disorder	(Barry et al., 2021)	USA	Experimental	Age: 18 - 60 years N =170
15.	Association of chronic non-cancer pain status and buprenorphine treatment retention among individuals with opioid use disorder: Results from electronic health record data	(John et al., 2022)	United States	Retrospective	Age: 18 years or older N = 676

Note: RCT: Randomized controlled trials

Quality Assessment

In this effort to develop rigorous, comprehensive quality analysis of this study, researchers established clear inclusion and exclusion criteria, developed a standardized form in which data was to be extracted, conducted an extensive review of every article, had discussions in peer review with a view to enhance neutrality, and reflected sensitivity analyses. The researchers were able to collect different opinions and resolve the contradictions based on the consensus by defining certain parameters in the selection of articles, using a structured data extraction form, critically evaluating the study design and methodology, and engaging the colleagues to help in quality assessment. Also, by investigating the effects of omission of lower quality articles using sensitivity analyses, the researchers made my findings reliable and stable.

Data Synthesis and Analysis

The findings of the studies included in the synthesis were summarized by a narrative synthesis method based on the inclusion criteria. Results were presented based on the themes to describe the relationship between Non-cancerous chronic pain and Opioid Use Disorder (OUD). A qualitative analysis of the data was performed where common themes and patterns among the studies could be discerned. A summary of the available evidence regarding the correlation of Non-cancerous chronic pain and Opioid Use Disorder (OUD) was provided in a logical and understandable manner.

Table 2

Assessment of Variables in the Reviewed Studies (N = 15)

Sr=No	CNCP	OUD	Other Constructs	Conclusion
1	ICD-9 codes	DSM 5	MED	Finally, the research showed that people in the age bracket of 60 years and older who took opioids at doses of 50 mg or more daily were more likely to fracture two times than people in the age bracket who stopped using opioids. This observation highlights a need to consider this augmented risk in prescribing escalated quantities of opioids to geriatric patients. More studies are needed on finding the relationship between the dosage of opioids and the risk of fracture in the elderly. Additionally, more studies are needed to determine whether greater rates of surveillance, adjustments in opioid dosage or non-pharmacological management of chronic pain would be helpful to minimize the risk of fractures in elderly patients. Such studies are also expected to ensure that pain is kept under control as per the preferences of the patients.
2	BPI-SF	BFI		The results of the two extension trials done in an open-label format lend support to the long-term efficacy and tolerability of the fixed combination of oxycodone PR (prolonged-release) and naloxone PR in the treatment of chronic pain. In the course of this effective analgesic treatment, the patients

					reported that they had significantly increased overall effects on daily activity due to pain. However, greater doses of opioids, and extended opioid use periods are associated with an increased likelihood of opioid abuse. This study also discussed role of multimodal management of chronic pain, which means using non-opioid medications, cognitive-behavioral therapy, physical activity, and other non-pharmacological methods to decrease opioid dependence.
3	BPI	COMM	PDUQ, POTQ	&	The validation of the COMM (Current Opioid Misuse Measure) was positive. Even though the values decreased marginally when applied on a completely new patient population, as would be natural, the predictive validity of the method as measured by the AUC (Area Under the Curve) was very significant. This suggests that the COMM could be a valuable tool for clinicians, enabling them to oversee instances of misuse and establish strategies for treatment to minimize ongoing misuse. Additionally, the COMM may serve as a useful tool for healthcare providers requiring documentation of their patient's ongoing adherence and proper utilization of opioids for the management of pain. The outcomes of this measure can also reduce the fears of both physicians and patients about opioid prescriptions and make them more aware of the need to use medications responsibly.
4	ICD-CM	ADRB			Over the course of 6 months, over fifty percent of all patients who received a 90-day opioid therapy program continued to take opioids after 90 days and extended to years of opioid use. These long-term opioid use rates are worthy to be considered and discussed before establishing Chronic Opioid Therapy with patients. Exposure to opioids in the past, 120 mg Morphine Equivalent Dose (MED) per day, or higher, and potential indicators of misuse were the variables revealing the strongest correlation with further opioid use. It should be mentioned, though, that the data that was utilized to establish these connections did not include any clinical assessments such as pain intensity or disease severity. Further precautions and steps in checking patients that undergo opioid therapy beyond 90 consecutive days may be advised, especially when using higher doses, or when showing potential signs of ill use.
5	OPCA	UDT			The aim of this paper was to review the practice of opioid prescription within a primary care setting, with the view of possibly applying the findings to improve provider knowledge on practices to manage chronic pain. The finding supports the hypothesis of opioids abuse in chronic patients because they have increased risk of opioid prescription and administration to treat enduring pain.
6	ICD-9-CM	DSM-5			Buprenorphine is difficult to administer orally, but can provide convenience, dosage flexibility, rapid action and sustained release. These attributes are especially significant to people with cancer, post-surgery or other chronic pain issues. Taking into account that the buprenorphine doses applied in pain treatment are not exceeding the typical ones, the integration of new delivery methods and technologies and the development of new options can potentially introduce new solutions to the problem of absorption and the issues associated with it.
7	BPI	DSM-IV-TR			The common occurrence and chronicity of psychiatric conditions, such as depression, mania or anxiety, that transpire in conditions of co-occurring chronic pain with opioid use disorder may be a contributing factor to the

				difficulties experienced by healthcare providers when working with such patients. The findings also suggest possible improvements of treatment by defining specific targets to be achieved in order to address co-occurring psychiatric disorders.
8	GPG	AUDIT-C,	QOL &PHQ,	Among the participants, those allocated to the higher dose reported the lowest proportion of problematic pain issues but the most common cases of problematic substance use on self-reporting. Conducting long-term follow-up on this cohort will allow for the assessment of how these factors impact clinical results.
9	GPG	COMM		To summarize our findings, our study revealed that 31.5% of patients in Germany who were receiving prolonged opioid therapy for chronic non-cancer pain (CNCP) displayed a high risk for aberrant drug behavior. It is important to note that this does not indicate addiction among these patients, although their risk may be heightened. Given the limitations of opioids (including their narrow therapeutic index and limited evidence supporting their efficacy in addressing different facets of chronic non-cancer pain), it is recommended that these high-risk patients receive regular follow-up and monitoring. Additionally, screening and addressing depression should be a routine practice in CNCP cases, considering its prevalence and the significant overlap between addiction risk and depression in this population.
10	DSM-5	DAST-10		In our sample, over 25% of patients had opioid use disorder (OUD), with 9.3% showing moderate to severe levels. The high prevalence of OUD underscores the need for ongoing monitoring and follow-up in chronic non-cancer pain (CNCP) patients to address potential OUD.
11	DSM-5.	COMM		In this study, the observed rate of opioid use disorder (OUD) in the patient sample aligns with previous research. However, the definition of OUD, tolerance, and withdrawal, in particular, may be varied and should influence the reported rates. It is important to know the reasons why patients use opioids to determine those who are more likely to develop OUD. The modified DEQ items should be tested in further research and our interpretation of opioid prescriptions in this population should be improved.
12	ICD codes	DAST-10	CCIS	People with serious mental illness, who are at an increased risk of opioid related problems, nonetheless get opioid prescriptions more often than people who do not have a mental illness health clinician may have the required expertise to lead pain assessment and management programs in these patients. However, more research is required to learn how successful the involvement of mental health workers in such programs can be.
13	VAS-craving & VAS-pain	DSM-5	DEQ	Overall, the findings of this prospective observational study show that the switch to buprenorphine/naloxone (BuNa) was beneficial to patients with chronic non-cancer pain (CNCP) and opioid use disorder (OUD). These results indicate that the chronic pain may be one of the factors that contribute to the changes in the reward and pain pathways in the brain predisposing to the development of OUD. BuNa is a promising new treatment modality that can help to overcome opioid misuse, craving, psychiatric symptoms, and pain perception in this group. However, further research is needed to validate these findings and identify the specific patient profiles that would benefit most from transitioning to BuNa, as some participants discontinued the study due to inadequate pain relief.

14	BPI	DSM-5		Prolonged utilization of opioids for pain management may lead to development of tolerance, physical dependence, and addiction. Individuals who are actively seeking treatment for both chronic pain and opioid use disorder (OUD), the order of condition onset seems to be linked to variations in psychiatric comorbidity. However, Subsequent investigations should involve a more extensive participant pool consisting of individuals actively seeking treatment for both chronic pain and opioid use disorder (OUD), is needed to systematically explore whether distinct pathways exist for the development of these simultaneous presence of chronic medical conditions. Additionally, it is important to investigate whether these pathways lead to potentially different clinical targets.
15	ICD-9-CM	COMM	DASS	The findings indicate that the existence of chronic pain unrelated to cancer alone cannot be considered a reliable predictor of the ability of patients with opioid use disorder to retain buprenorphine. However, healthcare providers should be aware of the association between chronic non-cancer pain (CNCP) and increased psychiatric comorbidity in individuals with opioid use disorder (OUD) when devising therapeutic plans. Further research is necessary to explore the impact of additional characteristics of CNCP on treatment retention.

Note: ICD-9-CM: International Classification of Diseases, 9 the revision, Clinical Modification, OPCA: Opioid Pain Care Agreement; VAS-craving and VAS-pain: Visual Analog Scale , UDT: Urine Drug Test, COMM: Current Opioid Misuse Measure, PDUQ: Prescription Drug Use Questionnaire, POTQ: Prescription Opioid Therapy Questionnaire, BPI: Brief Pain Inventory, QOL: Quality of life, PHQ: Patient Health Questionnaire, AUDIT-C, DAST-10 : Drug Abuse Screening Test-10, BFI: Bowel Function Index, BPI-SF: Brief Pain Inventory-Short Form, GPG: Chronic Pain Grade, MED: Morphine equivalent dose, DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, CNCP: Chronic Non-cancer Pain, CCIS: Charlson Comorbidity Index Score, behaviors , ADRB: Drug-Related Behaviors.

Findings and Discussion

Prevalence of Chronic Pain and Opioid Prescription

The data presented in this systematic review shows that the problem of chronic pain is universal and is associated with a considerable percentage of the population. Cohen and Lema (2020) assert in a research study that opioid use can be prescribed to chronic pain patients, which in turn results in subsequent development of opioid use disorder (OUD). Furthermore, in another study by Dahlhamer et al. (2018), it was estimated that in the United States alone there were roughly 50,000 adults who had chronic pain, i.e., pain that lasts at least three months. The impacts of those high rates of chronic pain were far-reaching in high cost of health care and low productivity. Alongside this, Cohen and Lema (2020) have also found that patients with chronic pain are more susceptible to opioid prescriptions.

Risk of Opioid Use Disorder in Chronic Pain Patients

Results of this systematic review suggest that individuals with chronic pain that take opioids to alleviate pain are at risk of developing opioid use disorder. Since sustained opioid use as a form of analgesia can lead to tolerance, physical dependence, and addiction as found in research by Robinson et al. 2018), this type of analgesic can lead to addiction.

A national-level survey of drug use and health indicated that out of all persons who used a prescription opioid in the past 12 months, more than 40% of those who misused prescription opioids met the criteria employed to gauge a substance use disorder. The close relationship between the development of opioid use disorder and opioid misuse is highlighted here (National Survey on Drug Use and Health, 2017).

Impact of Dosage and Duration of Opioid Use

According to the results of this thoroughly conducted literature review by Toce et al. (2018), the higher the dose of the opioid and the longer the duration of opioid use, the higher the risk of OUD and dependency. The use of higher doses of opioids in the treatment of chronic pain must be cautiously prescribed with consideration of the risks involved. Strang et al. (2020) also support the idea, as the authors examined the relationship between the dose of opioids and the onset of OUD in a large group of patients with chronic pain. The results were the more the dose of opioid that was given, the greater the risk of OUD. Therefore, this systematic review concluded that Opioid Use Disorder (OUD) could develop when high doses of this drug are used in the treatment of chronic pain.

Comorbid Mental Health Disorders and Opioid Misuse

In the course of this systematic review, it was established that chronic pain is frequently followed by the mental health issues of anxiety, depression, and post-traumatic stress disorder (PTSD). These comorbidities can be also linked to the development of opioid use disorder since these patients may want to use opioids to self-treat to alleviate not only physical but also emotional pain (Speed et al., 2018). Results of the Data on the National Epidemiologic Survey on Alcohol and Related Conditions identify significant relationships between psychiatric conditions like bipolar disorder, anxiety disorders, and major depression and higher rates of prescription opioid misuse resulting in opioid misuse disorder. These findings prove the close connection between misuse of opioids and other substances and mental health conditions (Hasin & Grant, 2015).

Transition from Acute Pain to Chronic Pain with Opioid Use

The second result of this systematic review is that chronic pain could sometimes develop as a result of opioid use to treat acute pain, including post-surgical or post-injury pain. In such situations, patients who started with opioids as an initial painkiller are likely to take it over the course of time, which further predisposes them to opioid misuse and addiction (Reznikoff, 2018). In like manner, Nadeau et al. (2021b) indicated that the use of opioids to manage acute pain could also promote the development of chronic pain in individuals, resulting in the extension of opioid use beyond the target timeframe and increasing the probability of opioid use and addiction.

Multimodal Strategies for Chronic Pain Management

Multimodal strategies to chronic pain management are reinforced in the literature in this systematic review. It also involves the use of non-opioid analgesic drugs, other non-pharmacological alternatives (physical therapy, cognitive-behavioral therapy, et cetera) with an aim of reducing the use of opioids (Carley and Oesterle, 2021). Similarly (Brackett et al., 2021) claimed that the combination of a variety of modalities in treating chronic pain is effective in relieving pain with minimal risks of prolonged opioid therapy.

Neurobiological Susceptibility to Opioid Use Disorder

Furthermore, the literature of the present systematic review revealed that Chronic pain may lead to alterations in the reward and pain pathways in the brain, predisposing ones to opioid use disorder upon opioid intake (Levis et al., 2021). This can further be explained as individuals with preexisting genetic or neurochemical factors that make them more susceptible to substance use disorder may face an increased susceptibility to developing Opioid Use Disorder (OUD), when they consume opioids to manage pain (Schuckit, 2016).

Conclusion

So this review that aimed to assess chronic non-cancer pain as a predictor of opioid use disorder indicates that not everyone using opioids for chronic pain will develop opioid use disorder, the risk is elevated in individuals with chronic non-cancer pain due to their condition and opioid properties. Healthcare providers use a multidisciplinary approach to chronic pain management in order to reduce this risk. This includes the application of other forms of therapy such as physical therapy, cognitive-behavioral therapy, non-opioid drugs, and procedures to reduce opioid dependence. There is a need to be accountable in terms of tracking and assessment of the risks and benefits of opioids and educate patients on the risks and benefits of opioids.

Limitations

There are a few limitations to note about this systematic review. First, there is the possibility that potential publication bias has influenced the choice of the studies since it is more likely that studies with significant findings will be published than those with weak results. Second, the variability in the data due to the heterogeneity of the included studies in the design, population, methodological approaches and outcome measures limits the generalizability of the results. Thirdly, the credibility of the review conclusions is dependent upon the quality of the individual studies that make up the review, and any limitations or biases in those studies can possibly affect the overall strength of the evidence. The review is silent on confounding factors associated with economic status and social status, access to healthcare services, and comorbidity that may influence correlation between chronic pain and Opioid Use Disorder (OUD). Finally, the findings might be generalizable only to specific populations or settings, since the studies included might have been specific to one or another demographic group or region.

Recommendations

We now can suggest a few directions for future research and practice, given the current constraints. First, more study designs from robust to diverse are necessary to confirm the cause and effect of chronic pain, opioid use, and the development of OUD to opioid use disorder (OUD). Second, there should be a focus on reducing heterogeneity for the consideration of comparable studies by standardization of the definitions, diagnostic criteria and outcome measures, which could lead to more accurate cross-study comparisons. Third, because treatment effectiveness and OUD risk are heavily influenced by socioeconomic and healthcare access, confounders such as these should be considered by researchers.

Fourthly, there is further need for research exploring these to all settings, including resource-limited and non-Western environments, to ensure the application of these findings to a variety of populations. Proper opioid prescribing and monitoring frameworks should be promoted by policymakers to limit the potential for misuse and dependence to develop, and, at last, clinicians need to follow a multimodal approach to pain management combining pharmacological, psychological and behavioural strategies.

Implication

In this systematic review, we use the latest literature published as of 2023, offering an up-to-date analysis of the literature on the connection between Non-cancerous chronic pain, opioid misuse, and addiction. Having two reviewers will provide credible findings because chances of bias are removed. The review identifies the need to develop a multidisciplinary approach to managing chronic pain at the lowest risk of Opioid Use Disorder (OUD). It is a combination of non-opioid pain medications, cognitive-behavioral therapy, therapeutic activities, and other non-pharmacological interventions. Smart prescribing, such as comprehensive pain evaluation, alternative treatment evaluation, and prescribing the lowest dose of medication over the shortest time, is advisable. Education of the patient regarding the risk of opioids, alternative pain management approaches and the need to make an informed decision is highly significant. Comorbidity screening (including psychiatric conditions, etc.) and integrated physical and psychological treatment plans should be considered. Constant observation, follow-up, and open communication with patients taking opioids could help identify problems and implement the necessary interventions in time. Additional studies and policy interventions can be discussed to help evaluate the effectiveness of the non-opioid interventions, to determine the sustainability of the interventions, and the reasonableness of responsible prescription. Moreover, designing addiction treatment centers and developing non-pharmacological interventions to combat pain is also a welcome development.

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