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Prevalence and management of chronic nonmalignant pain in palliative care populations: A systematic review

Lucy Kernick, M.B.B.S. (HONS.), F.R.A.C.P., F.A.CH.P.M.[1,2], Paul Glare, M.B.B.S. (HONS., 2ND CLASS), M.A. APPL. ETHICS (HEALTHCARE), M.MED. (CLIN. EPIDEMIOL.), F.R.A.C.P., F.A.CH.P.M., R.A.C.P., F.F.P.M., A.N.Z.C.A., F.A.C.P.[3], Annmarie Hosie, PH.D., R.N., M.A.C.N.[4,5,6], Annie Chiu, B.MED.SC., F.R.A.C.P.[2] and David W. Kissane, M.D., B.S., M.P.M., F.R.A.N.Z.C.P., F.A.CH.P.M., F.A.C.L.P.[1,7,8]

[1]School of Medicine, The University of Notre Dame Australia, Sydney, NSW, Australia; [2]Palliative Care Department, Mercy Health, Melbourne, VIC, Australia; [3]Pain Management Research Institute, University of Sydney, Sydney, NSW, Australia; [4]School of Nursing & Midwifery, University of Notre Dame Australia, Darlinghurst, NSW, Australia; [5]Department of Palliative Care, St Vincent's Health Network Sydney, Darlinghurst, NSW, Australia; [6]IMPACCT (Improving Palliative, Aged and Chronic Care through Research and Translation), University of Technology Sydney, Ultimo, NSW, Australia; [7]The Cunningham Centre for Palliative Care, St Vincent's Hospital Sydney, Darlinghurst, NSW, Australia and [8]Department of Supportive and Palliative Care, Cabrini Health, Monash University, Melbourne, VIC, Australia

Review Article

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Author for correspondence: Lucy Kernick, Department of Palliative Medicine, Mercy Palliative Care, 3 Devonshire Rd, Sunshine, VIC 3030, Australia.
Email: lucyk82@hotmail.com

Abstract

Objectives. To investigate the prevalence and current approaches to clinical management of chronic nonmalignant pain in patients referred to palliative care services.

Methods. A systematic review was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and registered with PROSPERO (CRD42021205432). Six databases were searched on 25 August 2020 and again on 11 July 2022: PubMed and Ovid MEDLINE, Elsevier Scopus, PsychINFO, the Cochrane Library, and CINAHL. Search included prevalence or intervention studies with patients who had chronic nonmalignant pain and were referred to palliative care services. Screening was undertaken independently by 2 reviewers.

Results. The searches returned 417 titles; subsequent screening identified 5 eligible studies, 4 from the USA and 1 from Hong Kong, including 2 cohort and 3 cross-sectional studies. Sample sizes ranged from 137 to 323, with a total of 1,056 patients. The prevalence of chronic nonmalignant pain ranged from 14% to 34% across different palliative care settings. There was significant crossover of pain types; 54% of patients with chronic no-malignant pain had additional cancer-related pain or cancer treatment–related pain. Opioids were used to manage stand-alone chronic nonmalignant pain for 39% of patients compared to 58% with mixed chronic nonmalignant pain and other pain diagnoses.

Significance of results. Five studies have documented the prevalence of chronic nonmalignant pain of 14–34% in palliative care. Further research including prevalence and treatment studies would provide clearer evidence for best practice management of chronic nonmalignant pain in the palliative care setting.

Introduction

The field of palliative care is establishing a role earlier in patients' life-limiting illnesses. Key studies in oncology have shown benefit in symptom management and quality of life to substantiate this (Zhuang et al. 2018). The move to introduce palliative care early in the nonmalignant chronic disease setting is also growing, broadening the range of patient diagnoses and disease trajectories managed by palliative care (Tassinari et al. 2016). As a consequence of early referral, some patients will be seen by palliative care clinicians many months to years prior to death. This shift brings certain challenges not previously faced by clinicians who historically saw only patients with cancer and/or very short prognoses. One such challenge is the management of patients with chronic pain (Jones and Kamal 2021). This can include patients with chronic nonmalignant pain or mixed pain diagnoses which include cancer-related pain and cancer treatment–related pain.

Pain management is a core component of palliative care. Fear of increasing pain and the desire to be pain free are common concerns stated by patients referred to palliative care services (Bhatnagar and Gupta 2016). Effective pain management remains a focus for the clinician with regard to clinical practice, research, and service delivery/benchmarking (Daveson et al. 2021). However, pain management in the palliative care setting has stemmed historically from

managing cancer pain, which is routinely treated differently to nonmalignant pain. In people with cancer, pain is generally managed through the early introduction of opioids and a focus on absolute pain reduction, as outlined in the European Society of Medical Oncology guidelines (Fallon et al. 2018). Achieving adequate pain control using pharmacological treatment approaches is considered standard practice for oncology patients (Kurita and Sjogren 2021).

Chronic pain is defined as pain existing for more than 3–6 months (Scholz et al. 2019). This is because it is beyond the time expected for an injury to heal and acute pain to resolve. Chronic pain can be due to ongoing tissue damage, as in the case of advanced cancer, or it can occur in the absence of demonstrable tissue damage, due to abnormal processing of signals in the somatosensory system in the spinal cord and brain. Chronic pain is associated with lower quality of life, significant psychological distress, and increased medical co-morbidities (Currow et al. 2015). The encounter with pain is a subjective experience of the sensory neural input modulated by a person's genetic predisposition, prior learning, and the current physiological, mood, and environmental state (Turk and Gatchel 2018). Furthermore, taking analgesics does not adequately address the distress and disability experienced by patients with chronic pain when there is no serious demonstrable tissue damage.

Chronic nonmalignant pain is a significant problem worldwide, documented to affect around 20% of the general population in the United States and almost half the adult population in the United Kingdom. Chronic pain is associated with worse quality of life and reduced health outcomes (Mathieson et al. 2020). The growing use of opioids for chronic pain has been identified internationally as an area of concern because of lack of long-term efficacy, long-term side effects, and excessive deaths and opioid diversion (McElyea et al. 2022). This has led to a focus on reducing opioid prescribing for chronic nonmalignant pain and increasing regulatory controls.

Given the prevalence of chronic nonmalignant pain across the population, it follows then that it will be experienced by at least the same proportion of patients referred to palliative care services, and possibly greater. Coexisting chronic nonmalignant pain can complicate management of new pains related to a life-limiting condition due to sensitization of the somatosensory system. Further, while person-centered care underpins both chronic pain management and palliative care, the management approach differs. Multidisciplinary pain clinics focus on the biopsychosocial approach in their treatment of chronic pain. This approach addresses any persistent tissue damage as well as the range of social and psychological contributors to the person's experience of pain. Inherent in such treatment is prioritizing optimal function; acknowledging pain is likely to persist rather than expecting resolution; and thus, promoting a philosophy of learning to live well despite the presence of pain. Elements of this approach include pain education and cognitive behavioral therapy to counteract any unhelpful thoughts and behaviors (Turk and Gatchel 2018). In contrast, palliative care begins with the understanding of a patient's life-limiting illness and the notion of relief of suffering. This latter approach has an inherent urgency and emotionality, which drives most clinicians to use pharmacological and supportive measures to rapidly relieve the pain. Engaging the patient in cognitive and psychological strategies to manage persistent pain is often secondary in palliative care.

The pain management of someone with a very short prognosis is likely to be similar, whether the pain is due to their cancer or chronic back pain, with the focus on analgesics. The clinical difficulty lies with those who have a longer prognosis and chronic nonmalignant pain as the main concern. It is these patients who may potentially benefit from non-pharmacological treatment modalities that are more patient-centered and responsive to psychological and social needs. The increasing concern regarding safety and management of opioid harm in the palliative care context was the topic of a recent Delphi study (Lau et al. 2022). Currently, there is limited evidence and guidance for clinicians on the assessment and management of patients with chronic pain who are receiving palliative care. Research into this area is needed (Hui et al. 2020).

Objective

The objective of this study was to review the evidence for the prevalence and clinical management of patients with chronic nonmalignant pain referred to palliative care services.

Methods

Design

A systematic review was registered on PROSPERO (CRD42021205432) and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Liberati et al. 2009).

Search strategy

Six databases including PubMed and Ovid MEDLINE, Elsevier Scopus, PsychINFO, the Cochrane Library, and CINAHL were searched on 25 August 2020 and repeated on 11 July 2022, using the following MeSH search terms: "chronic pain" OR "chronic nonmalignant pain" OR "chronic non-malignant pain" OR "chronic non cancer pain" OR "chronic non-cancer pain" OR "somatoform disorders" AND "palliative care" OR "terminal care" OR "palliative medicine" OR "hospice care" OR "end of life care" OR "terminally ill" AND "analgesics" OR "analgesia" OR "cognitive behavioural therapy" OR "physical therapy modalities" OR "exercise therapy" OR "pain management" OR "mind body therapies" AND "prevalence" OR "treatment outcomes" OR "quality of life." No limitation to the search was made for publication date or study type. An example of the search strategy is shown in Supplement 1.

Eligibility criteria

As per our objective, studies were included if they involved persons with chronic nonmalignant pain referred to palliative care services. In this review, palliative care services were those providing specialist palliative care to people with advanced cancer or other progressive life-threatening medical conditions, and chronic nonmalignant pain was defined by clinician review establishing likely nonmalignant causation. The scope of the search was limited to patients referred to palliative care services so that the literature was relevant to that specific clinical setting. Other inclusion criteria were (1) adult participants (i.e., aged 18 years or older); (2) prevalence studies or any form of management studies (pharmacological and non-pharmacological) or guidelines implementation; (3) sample size $N \geq 50$ to avoid qualitative-only or underpowered studies; and (4) published in English. Articles were excluded if they reported studies of cancer pain only or were commentaries or case reports.

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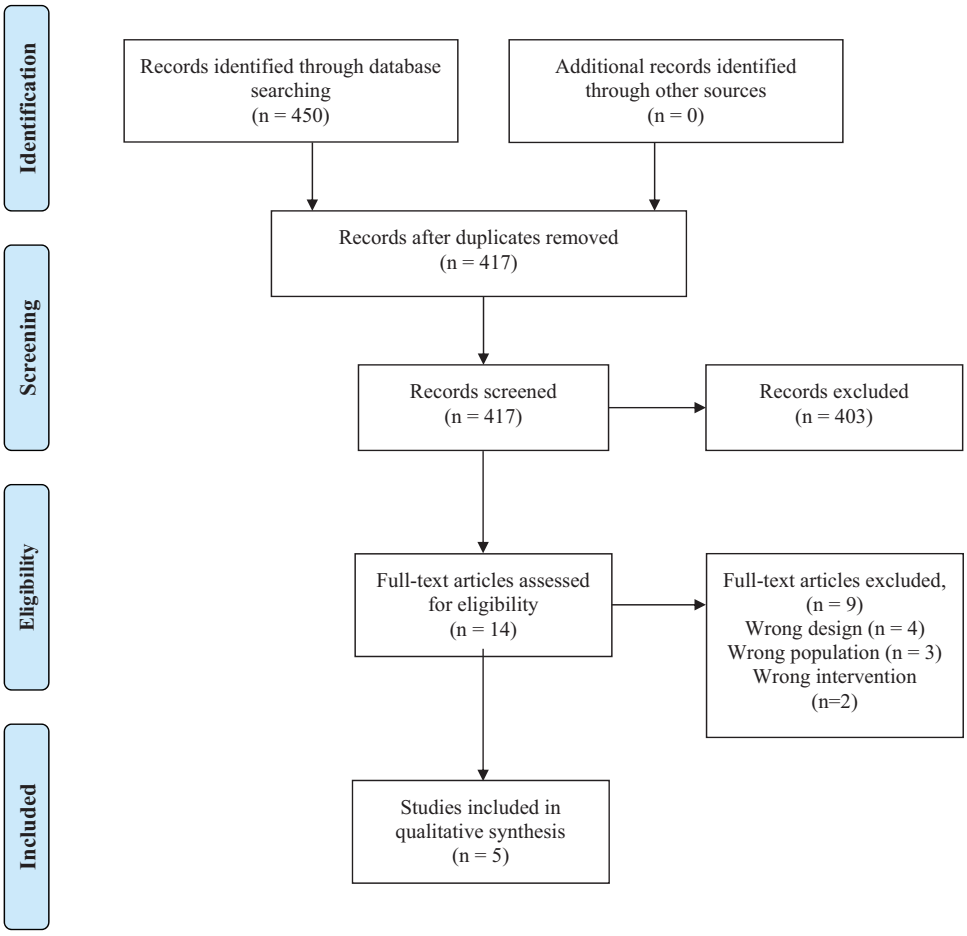

Fig. 1. PRISMA flowchart.

Study selection

Studies were independently screened in Covidence by 2 reviewers using the above inclusion and exclusion criteria. Initial screening was of title and abstract and then full texts were sourced for articles potentially meeting the eligibility criteria. Discrepancies regarding study inclusion were resolved by discussion.

Data extraction

Data extracted included study characteristics (place, year of publication, and setting); participant characteristics (gender, number, age, diagnoses, and cancer status if present); key diagnostic group's eligibility criteria, prevalence measures, and outcomes (chronic nonmalignant pain prevalence and treatment type/effectiveness); opioid usage, including doses expressed as total daily dose (TDD) in milligram oral morphine equivalents (OME), as documented by respective studies. Data were extracted into an Excel spreadsheet and reviewed by a second reviewer.

Risk of bias assessment

Risk of bias assessment was independently performed by 2 reviewers using the National Institute of Health's Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, comprising 14-questions plus an overall judgment as *poor, fair*, or *good* (National Heart 2021).

Data synthesis

Study data are summarized in a table, and prevalence and effectiveness measures and results were narratively synthesized, with mean/median summary estimates and associated ranges of numerical data provided. Meta-analyses were not possible given the heterogeneity of the included studies.

Results

The combined database searches returned 450 references, reduced to 417 after removing duplicates. Full text review of 7 articles identified 5 eligible articles, published between 2014 and 2020, that were included in this review (Figure 1).

Of the 5 included studies, 4 were performed in the United States (Childers et al. 2015; Hui et al. 2020; Jennings et al. 2014; Molony et al. 2014) and 1 in Hong Kong (Chan et al. 2018). All included studies were observational: 2 were cohort (Chan et al. 2018; Jennings et al. 2014) and 3 were cross-sectional studies (Childers et al. 2015; Hui et al. 2020; Molony et al. 2014). Two studies measured outcomes over time (initial visit and first follow-up) (Chan et al. 2018; Jennings et al. 2014). Three were supportive care clinics situated in cancer centers (Childers et al. 2015; Hui et al. 2020; Jennings et al. 2014); 1 was a renal supportive care clinic (Chan et al. 2018) and the other was a human immunodeficiency virus (HIV)/pain supportive care clinic (Molony et al. 2014). Sample sizes ranged from 137 to 323, with a total of 1056 patients.

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Each study measured patients' multiple pain types or diagnoses differently. One study (Chan et al. 2018) limited analysis to patient's "worst" pain only. Two studies documented up to 3 pain diagnoses per patient (Childers et al. 2015; Hui et al. 2020). One study documented only back pain (Molony et al. 2014), and one study did not comment on different pain diagnoses (Jennings et al. 2014). Pain assessment used the Edmonton Symptom Assessment Scale (Chan et al. 2018; Hui et al. 2020) in 2 studies and a Visual Analogue Scale/Numerical Rating Scales (Chan et al. 2018; Jennings et al. 2014) in 2 studies. One study did not use a pain measure, rather a clinician's assessment of aetiology (Molony et al. 2014).

Prevalence of chronic nonmalignant pain

Prevalence of chronic nonmalignant pain ranged from 14% to 34% across the studies (Table 1). A study of 200 patients in a supportive care clinic at a US comprehensive cancer center recorded up to 3 pain diagnoses per patient and found that 67 had chronic nonmalignant pain (34%) (Hui et al. 2020). There was a strong association between the number of pain diagnoses and the likelihood of chronic nonmalignant pain, the odds ratio of associated chronic nonmalignant pain if a patient has 3 diagnoses versus one being 75 (95% confidence interval 10.8–520.7, $p = 0.001$). In addition, there was a significant overlap in patients presenting with chronic nonmalignant pain, cancer-related pain, and cancer treatment–related pain: of 67 patients with chronic nonmalignant pain, 36 (54%) also had cancer-related pain or cancer treatment–related pain (Hui et al. 2020). Another US study of 323 patients of a supportive care clinic in an academic medical center reported that 87 (27%) had chronic nonmalignant pain and another 90 (28%) had no evidence of cancer disease (Childers et al. 2015). A study in a renal supportive clinic reported overall pain prevalence of 44%; of these patients, 49% had chronic pain (Chan et al. 2018). In a study in an HIV supportive care clinic which exclusively examined back pain, 55% of patients had back pain and 14% had chronic back pain (Molony et al. 2014).

Treatment of chronic nonmalignant pain

Types of treatment

Three studies reported opioid use, with all finding lower usage in chronic nonmalignant pain compared to cancer pain (Chan et al. 2018; Hui et al. 2020; Jennings et al. 2014). In the comprehensive cancer center, for the 361 pain diagnoses, patients with chronic nonmalignant pain were significantly less likely to be on opioids (30/94 [32%]) compared to patients with cancer treatment–related pain (28/60 [47%]) and cancer-related pain (120/182 [66%]; $p < 0.0001$) (Hui et al. 2020). In the academic medical center's cancer supportive care clinic, patients were already on high-dose opioids (average TDD > 300 mg OME) at initial assessment but trended toward lower doses in those with no evidence of cancer disease (mean 208.7 mg and SD 205.2 mg) and no life-limiting illness (mean 258.9 mg and SD 613.9 mg) compared with cancer pain (mean 393.1 mg and SD 463.1 mg, $p = 0.18$) (Jennings et al. 2014). The renal supportive care clinic study reported low rates of strong opioid prescription (3%), with simple analgesics used in 92% of patients and weak opioids in 29%. (Chan et al. 2018)

Response to opioids

Only 2 studies evaluated treatment outcomes, each at or around 1 month (Chan et al. 2018; Jennings et al. 2014). Both studies included adjuvant analgesics as well as opioids. Neither study documented any non-pharmacological treatments, nor described the overall components of the supportive care provided. The first study was that set in the renal supportive care clinic (Chan et al. 2018). This study used the Edmonton Symptom Assessment Scale score pre and post review to measure treatment response to weak or strong opioids according to the World Health Organization ladder in the subset with moderate–severe pain, although they did not distinguish between acute and chronic pain. The overall change in mean scores was reduced from baseline 4.5 (SD 1.9) to 2.3 (SD 2.2) ($p < 0.05$). For those with moderate to severe pain (>4), the treatment response was greater: baseline 5.8 (SD 1.9) to 2.9 (2.5) ($p = 0.007$) (Chan et al. 2018). The second study measuring treatment outcome was in an academic medical center's cancer supportive care clinic (Jennings et al. 2014). Opioid doses were titrated, and 6–20% of patients showed no statistical difference in opioid dosing at initial or first review ($p = 0.28$). The documented treatment included medication management involving opioid and non-opiate analgesia. This study defined treatment responders as those with a 2-point reduction in the Numerical Rating Scale or at least 30% reduction from baseline. An overall treatment response of 44% was reported; the greatest response was in patients with active cancer (57.4%) compared to those with no life-limiting illness (41%) and no evident disease (20%) ($p = 0.0091$) (Jennings et al. 2014).

Measures of alcohol or opioid misuse

Two studies measured alcohol dependence and risk of opioid misuse (Childers et al. 2015; Hui et al. 2020). Alcohol dependence was measured by versions of the Cut down–Annoyed–Guilt–Eye-opener (CAGE) tool in 2 studies (Childers et al. 2015; Hui et al. 2020). Risk of opioid misuse was assessed using 2 versions of the Screener and Opioid Assessment for Patients with Pain (SOAPP) tool in 2 studies (Childers et al. 2015; Hui et al. 2020). One study reported no difference in alcohol dependence or risk of misuse for those with chronic nonmalignant pain and the overall population (Hui et al. 2020). The other study found that 46% of all new patients had an elevated risk of opioid misuse according to SOAPP; however, the CAGE assessment indicated low rates of alcohol dependence (Childers et al. 2015). The risk of opioid misuse in the latter study was associated with younger age (50 vs. 61 y; $p = 0.007$) (Childers et al. 2015).

Risk of bias assessment

Regarding risk of bias, all 5 studies were assessed as "fair" on the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (National Heart, Lung and Blood Institute 2021) (Figure 2 and Table 1). All studies were at high risk of detection bias due to use of a single tool for pain assessment. Three studies recorded only one type of pain diagnosis per patient, and the effect of this potential confounder was not addressed in those studies. Four of the 5 studies were at a single site, where referral and patient characteristics were unique, limiting generalizability. Four out of 5 studies did not report sample size calculations or precision estimates in study design. The overall risk of bias is presented in Figure 2.

Discussion

This systematic review of the prevalence and management of chronic nonmalignant pain in patients receiving palliative care

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Table 1. Study characteristics

Authors (year)	Country	Aims	Design/setting/risk of bias	Participants	Measures	Results
Hui et al. (2020)	USA	To examine the prevalence and management of CNMP in cancer patients referred to SCC	Prospective cross-sectional study/SCC at single cancer center/+	*Eligible*: initial consultation at clinic[a], age ≥18 y, cancer diagnosis (with or without evidence of current disease), pain lasting for 3 months, no delirium *Participated:* $n = 200$, 47% male, mean age 60 y	ESAS, BPI, CCI CAGE-AID, SOAPP-14 Up to 3 pain diagnoses recorded	*Prevalence CNMP*: 34% (CI 28–41) *Secondary outcomes*: 39% patients with only CNMP on opioids
Chan et al. (2018)	Hong Kong	To examine the prevalence, severity, and management of pain in patients with advanced CKD attending renal SCC	Cohort study/Initial and follow-up at 1 month/Renal SCC-2 sites/+	*Eligible*: advanced CKD (KDOQI), conservative management only, symptomatic CKD or prognosis <1 y, age ≥18 y *Participated:* $n = 253$, male 51%, mean age 80 y	VAS, modified ESAS, PPS v2, first follow-up at 1 month with repeat ESAS	*Prevalence CNMP*: 22% *Secondary outcomes*: Treatment response (>2 point drop ESAS) in 53% ($p < 0.001$) at follow-up Neuropathic pain associated with poor pain treatment response at follow-up
Childers et al. (2015)	USA	To examine the prevalence of chronic pain and risk of opioid misuse in a palliative care clinic	Cross-sectional study/Single palliative care clinic located in a cancer center/+	*Eligible*: all patients presenting to the clinic *Participated*: pain analyzed for all patients $n = 323$, new patients with opioid misuse measures $n = 57$, male 50%, mean age 54 y	CAGE, SOAPP-SF, urine drug screen as requested, aetiology of pain clinician assessed	*Prevalence non-cancer pain*: 27% *Secondary outcome*: Risk of opioid misuse: 46% positive score of 4 or more on the SOAPP, 15% positive CAGE score. Of the 4% who had urine drug screening ($n = 27$), 15 (56%) had aberrant results
Jennings et al. (2014)	USA	To determine the response to treatment of pain in patients seen at SCC divided into AC, NED, NLLI	Cohort study/SCC at single cancer center/+	*Eligible*: all patients presenting to SCC *Participated:* $n = 143$, matched data in 94 analyzed for treatment response, male = 46%, mean age 51 y	VAS, MEDD 24-h initial and first follow-up (median 29 days) Responders ≥2 pts or 30% reduction VAS	*Prevalence CNMP*: 19.6% NLLI (additional 24.5% NED) *Secondary outcomes*: No difference in opioid doses between groups; highest treatment responders in AC 57.4%, NED 20%, NLLI 41% ($p < 0.05$) Benzodiazepine use is highest in NLLI
Molony et al. 2014	USA	To describe patients referred to chronic pain focused on HIV/SCC with back pain and associated imaging	Cross-sectional study/HIV SCC at HIV center/+	*Eligible*: in AIDS research study[b], age ≥19 y, first appt within study time, completed ≥1 outcome survey *Participated:* $n = 137$, male 71%, mean age 45 y	PROM, PHQ-9, PHQ-9A, Use of MRI and clinician assessment	*Prevalence chronic back pain*:14% *Prevalence acute/chronic back pain*: 55% *Secondary outcomes*: 29% of those with back pain had MRI of the lumbar spine and 3% had malignancy

Overall risk of bias assessment: poor (0), fair (+), good (++)

[a]Multiple pain types per person, so % > 100 (361 pain diagnoses in 200 pts)

[b]Center for AIDS Research Network of Integrated Clinical Systems prospective cohort study (includes >90% clinic pts)

AC = active cancer, BPI = brief pain inventory, CAGE-AID = cut down–Annoyed-Guilt–Eye-opener–Adapted to Include Drugs, CCI = Charlton Comorbidity Index, CKD = chronic kidney disease, CNMP = chronic nonmalignant pain, ESAS = Edmonton Symptom Assessment Scale, HIV = human immune deficiency, K/DOQI = Kidney Disease Outcome Quality Initiative, MEDD = Morphine Equivalent Daily Dose, MRI = magnetic resonance imaging, NED = no evident disease, NLLI = no life-limiting illness, NRS = numerical rating scale, PHQ-9 = Patient Health Questionnaire-9, PHQ-9A = Patient Health Questionnaire-9Anxiety, PROM = Patient Reported Outcome Measures, pts = patients, SOAPP-14 = Screener and Opioid Assessment for Patients with Pain-14, SOAPP-SF Screener and Opioid Assessment for Patients with Pain v 1.0 – short form, SCC = supportive care clinic, VAS = Visual Analogue Scale, y = years

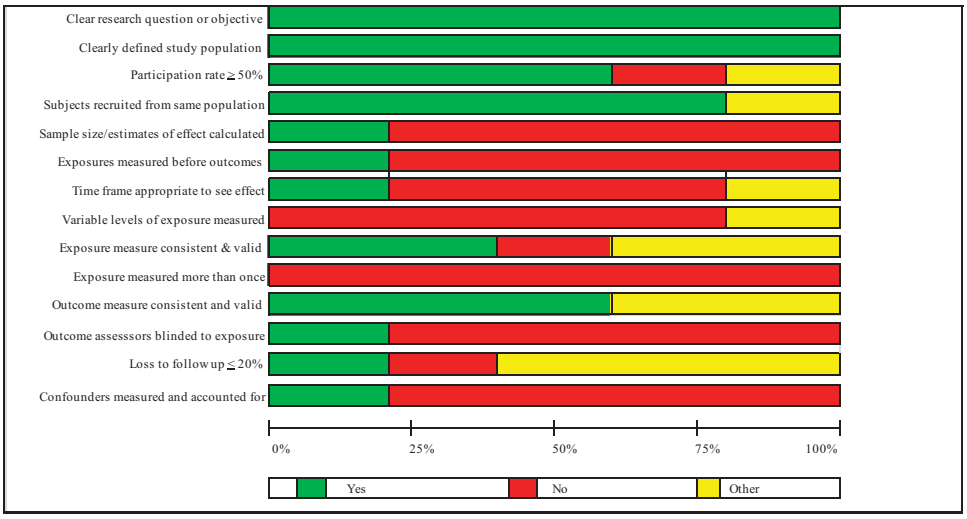

Fig. 2. Risk of bias assessment.

revealed few relevant studies. The prevalence of chronic nonmalignant pain was found to be between 14% and 34% across a range of supportive care clinic populations. Lower rates of opioid analgesics were reported for patients with chronic nonmalignant pain. However, opioid use was common in these patients; the range of use was 39–58%, depending on the coexistence of cancer-related or cancer treatment–related pain. The risk of opioid misuse was estimated at 46% of patients in one study (Childers et al. 2015).

This review highlights the difficulty in isolating chronic nonmalignant pain from a patient's overall experience of pain. Up to half the patients with chronic nonmalignant pain had comorbid cancer-related or cancer treatment–related pain. Differences in the number of pain diagnoses studied raised the question of missed chronic nonmalignant pain diagnoses, especially when malignant pain was the focus of the study. While one study documented up to 3 pain diagnoses or types, the other studies did not assess multiple pain types experienced by patients. The clinical picture and subsequent management decisions are challenging, given the mixed nature of pain and the fact that patients can experience multiple pain types or diagnoses currently.

While one might question the attention on pain diagnoses or causation in the palliative setting, the lessons from chronic pain research are important to heed. The benefit of opioid prescription and dose escalation in the chronic pain setting is limited; the updated Centers for Disease Control and Prevention (CDC) guideline recommends dose reduction and avoidance of opioids wherever possible (Dowell et al. 2022). Opioid prescription can be associated with misuse and can have significant side effects, which have historically been minimized in palliative care settings where cancer pain predominated and prognosis was short.

Patients have long been concerned with analgesic side effects and sought more use of non-pharmacological approaches to pain management (Jennings et al. 2014). In the oncology setting, goals of care toward the end of life have focused on sustaining the quality of life and reducing suffering. The immediate reduction of pain, with analgesics and other treatment modalities, has been a target for most clinicians. Even here, the need for careful education, enhanced communication, personalized care, and the use of non-pharmacological approaches have been called for (Azizoddin et al. 2021). When we look to a future where palliative medicine contributes to more non-oncological care and earlier involvement with patients long before the terminal phase, the management of patients with chronic nonmalignant pain requires whole-person care alongside relief of their distress and morbidity.

This review shows the limited research that has been done into this evolving area of palliative care. The management of patients with both chronic nonmalignant pain and life-limiting illness is complex and is currently left out of both chronic pain and palliative care guidelines, respectively. The prevalence of chronic nonmalignant pain in these studies mirrors that of the general population, where chronic pain estimates are increasing. Future research into the intersection of chronic nonmalignant pain and palliative care is timely and would inform an evidence-based approach to best clinical care for these patients.

Limitations

The studies included in this review had small, cross-sectional samples from single outpatient sites and nearly all were conducted in the US. Pain assessment was generally limited to a single numerical screening tool. There was no attention to psychological components of pain, associations of which have been shown to be significant in the chronic pain literature. The modality of diagnosis of nonmalignant pain was only described in 2 studies. The medication history was documented in only 3 studies, and of them opioid and non-opioid medications were reported in only 2. The result is a heterogeneous picture which restricts generalization, and the study quality was assessed as fair. Some institutions lack a comprehensive chronic pain service, causing pain referrals to be made to palliative care programs, which are not necessarily staffed to respond to chronic pain. In addition, we included studies in renal supportive and HIV/pain supportive clinics, which are clearly specialized and increased the heterogeneity of the studies reviewed.

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Conflicts of interest. The authors report no conflict of interest.

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