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Review Article

The Prevalence of Opioid Analgesic Use in People with Chronic Noncancer Pain: Systematic Review and Meta-Analysis of Observational Studies

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Abstract

Objective. To review studies examining the proportion of people with chronic noncancer pain who report consuming opioids and characteristics associated with their use. **Design.** Systematic review. **Methods.** We searched databases from inception to February 8, 2020, and conducted citation tracking. We included observational studies reporting the proportion of adults with chronic noncancer pain who used opioid analgesics. Opioids were categorized as weak (e.g., codeine) or strong (e.g., oxycodone). Study risk of bias was assessed, and Grading of Recommendations

Assessment, Development and Evaluations provided a summary of the overall quality. Results were pooled using a random-effects model. Meta-regression determined factors associated with opioid use. **Results.** Sixty studies (N=3,961,739) reported data on opioid use in people with chronic noncancer pain from 1990 to 2017. Of these 46, 77% had moderate risk of bias. Opioid use was reported by 26.8% (95% confidence interval [CI], 23.1–30.8; moderate-quality evidence) of people with chronic noncancer pain. The use of weak opioids (17.3%; 95% CI 11.9–24.4; moderate-quality evidence) was more common than the use of strong opioids (9.8%; 95% CI, 6.8–14.0; low-quality evidence). Meta-regression determined that opioid use was associated with geographic region (P=0.02; lower in Europe than North America), but not sampling year (P=0.77), setting (P=0.06), diagnosis (P=0.34), or disclosure of funding (P=0.77). **Conclusions.** Our review summarized data from over 3.9 million people with chronic noncancer pain reporting their opioid use. Between 1990 and 2017, one-quarter of people with chronic noncancer pain reported taking opioids, and this proportion did not change over time.

Key Words: Opioid Analgesics; Chronic Pain; Systematic Review

Introduction

Chronic noncancer pain affects approximately 20% of people worldwide [1], and the prevalence increases with age and female gender [2, 3]. Chronic noncancer pain has a substantial impact on society by costing billions of dollars each year in health care costs and lost productivity [3]. A common cause of chronic noncancer pain includes chronic low back pain, the leading cause of years lived with disability globally [4].

Opioid analgesics are commonly used to manage chronic noncancer pain. Current clinical practice guidelines for the management of chronic noncancer pain, such as those from the Centers for Disease Control and Prevention [5], now recommend avoiding the initial use of opioid analgesics, as the risk of harms, such as overdose and death [5], frequently do not outweigh the benefits. Changes in clinical guideline recommendations may reduce the number of opioid prescriptions issued to patients with chronic noncancer pain. However, considering that not all prescriptions are filled [6], estimates from prescription data do not equate to the actual consumption of medicines. Nonadherence to opioid analgesics prescribed to patients with chronic pain is as high as 50% [7].

The global use of opioid analgesics in general doubled between 2001 and 2003 to between 2011 and 2013 to 7.35 billion daily doses per annum, predominantly driven by increases in North America, Europe, and Oceania [8]. The use of opioids in people with chronic noncancer pain has been reported by individual studies [9, 10], but there has yet to be a systematic overview of such studies. Although the proportion of people with chronic noncancer pain being prescribed an opioid has increased over time [11], it is unclear from the literature whether the consumption of opioids has also increased over time. Furthermore, some types of opioids may be used more frequently, or opioid use may vary between different clinical settings and geographic locations. Establishing the extent to which opioid analgesics are used by people with chronic noncancer pain is important, as the available studies that measure prescription rates may overestimate or underestimate actual opioid analgesic use. The aim of this systematic review was to investigate studies examining the proportion of people with chronic noncancer pain who report using opioid analgesic medicines and the type(s) of opioids used. We also considered whether study estimates were influenced by factors such as the year(s) the study was conducted.

Methods

This systematic review was prospectively registered (PROSPERO CRD42017063957; www.crd.york.ac.uk) and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [12] and Meta-Analysis of Observational Studies in Epidemiology [13] guidelines.

Eligibility

Observational studies reporting the number of adults (≥18 years) with chronic noncancer pain who report taking opioid analgesics to manage their pain were considered for inclusion. Opioid use included the self-reported use of any type of opioid analgesic, at any dose and for any duration, and collected data on opioid use over any period of time. Studies were required to be of a representative sample—e.g., randomly sampled from the electoral roll but not required to be of a national sample. Studies using secondary data such as reports from administrative data on opioid use (not prescription data) were also eligible. We included studies of chronic noncancer pain in one or more body locations (e.g., musculoskeletal pain, fibromyalgia) for at least 3 months. Studies that reported the prescription of nonopioid therapies only, opioid dispensing or prescription data (i.e., issuing of prescriptions from medical records), studies involving only pregnant women, or studies conducted entirely on chronic conditions related to visceral causes (e.g., gastroesophageal reflux disease or stable angina) were excluded.

Search Strategy

The PubMed (NLM®), MEDLINE (OvidSP), EMBASE (OvidSP), Web of Science (Thomson Reuters), and

International Pharmaceutical Abstracts (OvidSP) databases were searched from individual database inception to February 8, 2020. The full search strategy is detailed in Supplementary Data. Additionally, backward and forward citation tracking of included papers was conducted (Scopus and PubMed [NLM®]), and we communicated with content experts to identify missing studies. There were no language or publication date restrictions.

Screening

Two authors (Graeme Wertheimer and Stephanie Mathieson) independently screened titles and abstracts. The full text of potentially eligible studies was independently appraised to determine their inclusion. Disagreements were resolved by discussion and then arbitration by an independent review author when needed (Christopher G. Maher). For articles written in languages that could not be read by review authors, we sought assistance from colleagues in reading the articles.

Data Extraction and Management

Two authors (selected from Stephanie Mathieson, Graeme Wertheimer, Chung-Wei Christine Lin, Andrew J. McLachlan, Rachelle Buchbinder, Sallie-Anne Pearson, and Martin Underwood) independently extracted data from each study. Disagreements were resolved by discussion and then arbitration by an independent review author (Christopher G. Maher) if necessary. We contacted study authors for clarification and additional data when necessary.

Data were extracted on standardized and piloted data extraction forms. Information extracted included bibliometric data (e.g., date of publication); study characteristics (e.g., sampling methods); participants (e.g., chronic pain diagnosis); and opioid regimen (e.g., proportion used, type, dose regimen).

Medicines were classified following the Anatomical Therapeutic Chemical classification [14]. Opioid analgesics were then categorized as 1) weak (codeine, tramadol, dihydrocodeine, dextropropoxyphene, and tilidine) or 2) strong (e.g., oxycodone, morphine, pethidine, fentanyl, hydromorphone, buprenorphine, tapentadol). The combination was categorized as a weak (e.g., codeine plus acetaminophen) or strong combination opioid analgesic (e.g., oxycodone plus acetaminophen). Opioids were not categorized further into long-acting or short-acting drugs.

Setting was categorized into primary care (e.g., general practitioner); secondary care (e.g., hospital, emergency department, and medical specialists); tertiary care (e.g., multidisciplinary pain treatment programs); general population; or database (e.g., Veterans Affairs, insurance claims databases).

Countries were classified into regions according to the World Health Organization (WHO) as Africa; Americas (Northern, Central, and Southern); Europe; Southeast Asia; Eastern Mediterranean; and Western Pacific [15]. Countries were also classified as low-income, middle-income, or high-income countries according to the World Bank [15].

Risk-of-Bias Assessment

Two reviewers (selected from Graeme Wertheimer, Stephanie Mathieson, Chung-Wei Christine Lin, Andrew J. McLachlan, Rachelle Buchbinder, Sallie-Anne Pearson, and Martin Underwood) independently assessed the risk of bias of eligible studies. Disagreements were resolved by discussion and then arbitration by an independent review author if necessary (Christopher G. Maher). Risk of bias was assessed using a modified risk-of-bias tool developed by Hoy et al. [16] designed to assess the risk of bias of prevalence studies. The assessment criteria and scoring are presented in Supplementary Data.

Strategy for Data Synthesis

The screening and selection of studies was summarized in a diagram following the PRISMA recommendations [12]. The study and participant characteristics are reported descriptively. Dichotomous variables (e.g., opioid use) are reported as proportions, n/N (%). The extent (prevalence) of opioid use was determined as the proportion of people with chronic noncancer pain who reported taking an opioid over any time period. Some studies provided estimates for opioid use per year over multiple years. As we wanted to evaluate if opioid use changed over time, we extracted estimates for opioid use per year, with some studies providing estimates for multiple years. Continuous outcomes were reported as means with 95% confidence intervals (CIs) if thse intention was to describe precision of an estimate or the standard deviation (SD) if the intention was to describe sample variability. Where possible, outcomes were converted to a common metric to aid comparison (e.g., opioid dose converted to morphine milligram equivalents [MME] per day) [6].

When study data were sufficiently statistically homogeneous ($I^2<50\%$), study results were combined in a meta-analysis using a random-effects model irrespective of setting or chronic noncancer pain diagnosis. The pooled estimates with 95% CIs are presented using forest plots. Heterogeneity was assessed by visual inspection of the forest plot (e.g., *P* values and overlapping CIs) and the I^2 statistic. We considered the interpretation of the I^2 as per the *Cochrane Handbook for Systematic Reviews of Interventions*: 1) 0% to 40% might not be important; 2) 30% to 60% may represent moderate heterogeneity; 3) 50% to 90% may represent substantial heterogeneity; and 4) 75% to 100% may represent considerable heterogeneity. Meta-regression explored study-level factors associated with the estimates of opioid use and heterogeneity. Factors included in the model were 1) year (the midpoint [year] of the study period from which the opioid estimate was sampled); 2) WHO region

(North America [reference], Eastern Mediterranean, Europe, Southeast Asia, and Western Pacific); 3) setting of data sampling (general population [reference], database, primary care, secondary care, tertiary care); 4) chronic pain diagnosis (headache or migraine, low back pain, fibromyalgia, inflammatory arthritis, osteoarthritis, phantom limb pain, chronic pain from spinal cord injury, chronic noncancer pain [reference]); and 5) if study funding was disclosed (yes or no [reference]). There were insufficient data to assess participant-level factors within studies. We used a two-sided *P* value Hartung–Knapp maximum-likelihood method. Analyses were conducted in Comprehensive Meta-Analysis Software version 3 [17]. When data could not be pooled, we performed a narrative synthesis.

A Grading of Recommendations Assessment, Development and Evaluation (GRADE) [18] approach provided a summary of the overall quality of evidence. The GRADE assessment criteria and scores are presented in Supplementary Data.

Subgroup and Sensitivity Analyses

We repeated the aforementioned analyses on the subset of data for people with chronic low back pain. Three sensitivity analyses were conducted on the pooled opioid estimate in people with chronic noncancer pain. The first analysis removed studies with a high risk of bias. The second analysis considered tramadol a "strong opioid" rather than a "weak opioid." This recognized differences in the scheduling of tramadol between countries (e.g., tramadol is considered a "strong opioid" in the UK [19] but a "weak opioid" in other countries such as Australia [20]). The third analysis considered the length of time opioid use was reported in the data collection. We grouped opioid use as current opioid use (reporting opioid use between the day of survey and the previous month) or past opioid use (opioid use from more than 1 month ago to the last 2 years [the longest time identified from included studies]), irrespective of a participant's duration of treatment or previous opioid use. The length of opioid use was included as a covariate in a post hoc meta-regression model.

Results

Search Results

There were 34,347 citations identified by the search, of which 60 studies were included. The flow of studies is presented in Figure 1.

Included Studies

Sixty studies (n=3,961,739 participants) reported data on opioid use from 1990 to 2017. Studies were published from 1997 to 2019. Studies were mainly from the United States (n=33) [10, 21–53], with other studies from Australia [54–56], Belgium [57], Brazil [58], Canada [59], Chile [60], England [61], Denmark [9, 62–67], Germany [68, 69], India [70], Iran [71, 72], Israel [73], Norway [74], Portugal [75], Spain [76], The Netherlands [77], and/or from multiple countries (France, Germany, Italy, Spain, the UK) [78]. Four studies were from middle-income countries [58, 70–72], and no studies were from low-income countries. Approximately half the studies (n=31) were of specific chronic noncancer pain subpopulations, most commonly low back pain [10, 25, 28, 31, 32, 35, 38, 46, 48], followed by fibromyalgia [40, 43, 44, 51, 53, 68], osteoarthritis [29, 32, 35, 39, 45, 77, 78], headache [21, 23, 24, 58, 67, 76], and rheumatoid arthritis [27, 35, 37]. The details of the included studies are provided in Table 1.

Risk of Bias

The risk-of-bias scores are presented in Supplementary Data. Twelve studies were judged to be at low risk of bias (20.0%). The majority of studies were considered to have moderate risk of bias (77%, n=46 studies). The item considering the reliability and validity of the instrument used to measure opioid use was frequently judged to have high risk of bias, as most studies retrospectively reviewed opioid use from clinical records rather than using validated measures.

Opioid Analgesic Use

There was moderate-quality evidence that the proportion of people with chronic noncancer pain who used an opioid was 26.8% (95% CI, 23.1–30.8; n=60 studies; Figure 2). Mean opioid dose across studies was unable to be determined, as 91.6% of studies did not report daily dose consumed. Of the five studies reporting dose [28, 34, 36, 62, 69], the mean opioid dose ranged from 36.9 MME/d (SD, 34.7) [34] to 244.6 MME/d (SD, 185.7) [28]. The types of opioids used by people with chronic noncancer pain were reported in 17 studies. There was moderate-quality evidence that a weak opioid was used by 17.3% (95% CI, 11.9–24.4; n=17 studies) [10, 23, 25, 26, 31, 32, 44, 53, 55, 59, 63, 64, 67, 73, 75, 76, 79] and low-quality evidence that a strong opioid was used by 9.8% (95% CI, 6.8–14.0; n=16 studies) [10, 23, 25, 26, 31, 44, 53, 55, 59, 63–65, 67, 73, 75, 79] of people. A small number of studies reported opioid combination analgesic products. There was moderate-quality evidence that the use of weak opioid combination preparations by people with chronic noncancer pain was 2.7% (95% CI, 2.2–3.2; n=4 studies) [58, 64, 67, 75], and one study reported with moderate-quality evidence that the use of strong combination preparations was 5.0% (95% CI, 2.5–9.7) [64].

Factors Associated with Opioid Analgesic Use

A meta-regression model explained 53% of the variance of reported opioid use in people with chronic noncancer pain (R^2 = 0.53). The WHO region (*P*=0.020; Europe

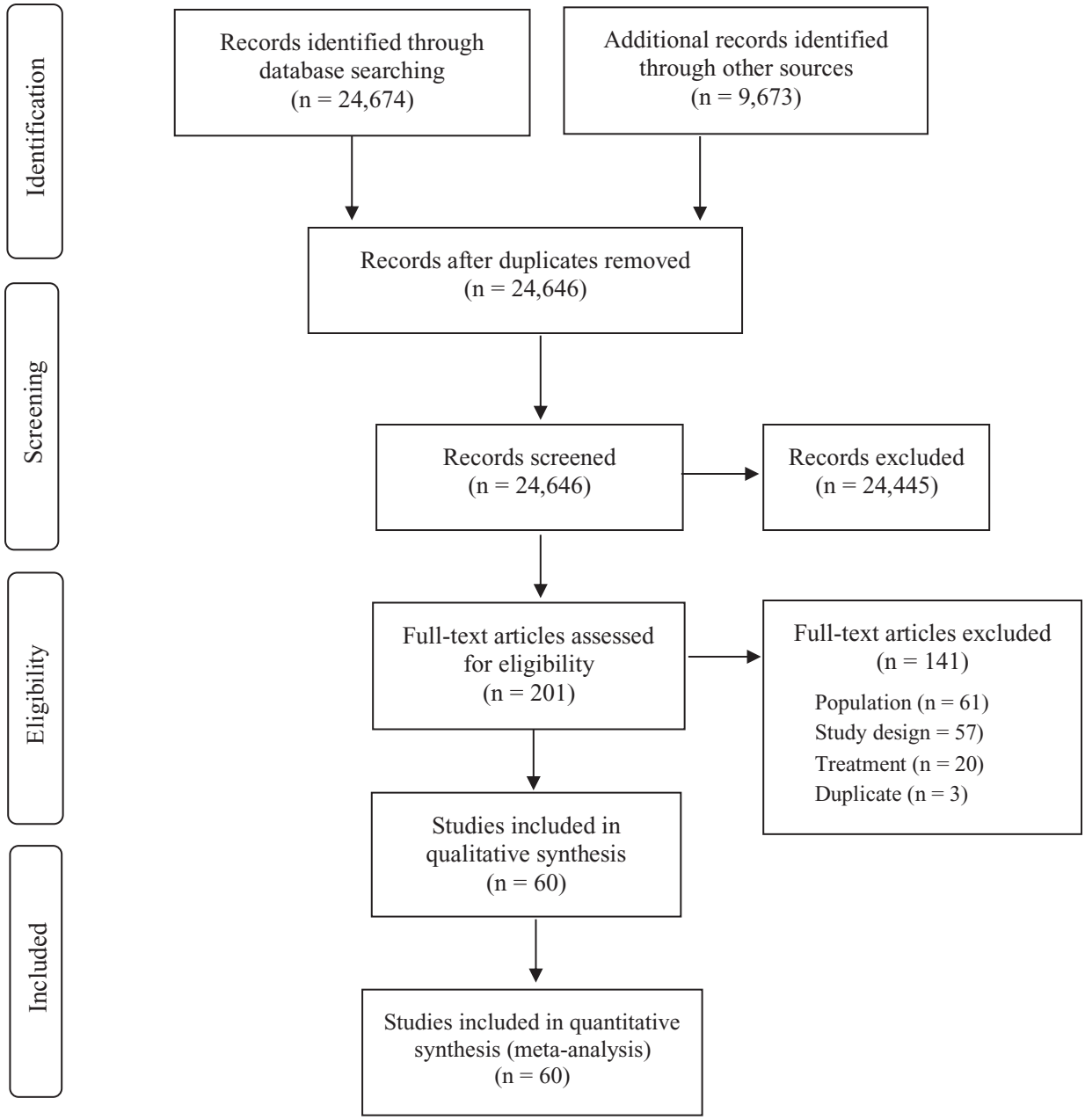

Figure 1. Study flow of study screening and eligibility.

[P=0.002] compared with North America [reference]) was significantly associated with less opioid use, but not the year of data collection (from 1990 to 2017) (P=0.770), setting of data collection (P=0.064), chronic pain diagnosis (P=0.341), or whether funding was disclosed (P=0.077). The adjusted estimates of opioid use over time and the detailed meta-regression results are presented in Supplementary Data.

Subgroup Analyses

Eight studies (13%) reported the use of opioid analgesics in people with chronic low back pain. There was moderate-quality evidence that 29.8% of people with chronic low back pain (95% CI, 20.5–41.2; n=8 studies) [10, 25, 28, 35, 38, 46, 48, 75] used an opioid analgesic (Supplementary Data). Three studies reported the types of opioids used by people with chronic low back pain [10, 25, 54]. There was moderate-quality evidence from two studies [10, 25] that weak opioids were used by 3.1% of people with chronic low back pain and low-quality evidence that strong opioids were used by 28.6% of people with chronic noncancer pain [10, 25]. The other study reported both weak and strong opioid analgesic combination opioid products [54].

A meta-regression model determined that sampling year and geographic region were not associated with the use of opioid analgesics in people with chronic low back

Table 1. Characteristics of included studies

Author	Country	Sampling Year	Study Design	Setting	No. of Participants	Pain Complaint
Azevedo, 2013 [75]	Portugal	2007–2008	Cross-sectional	General public	2,213	Chronic noncancer pain
Becker, 1997 [62]	Denmark	1994–1995	Cross-sectional	Tertiary care	150	Chronic noncancer pain
Bigal, 2008 [21]	United States	2004–2009	Longitudinal	General public	209	Chronic headache
Bilbeny, 2018 [60]	Chile	2013	Cross-sectional	General public	278	Chronic noncancer pain
Birke, 2016 [9]	Denmark	2000, 2005, 2010, 2013	Cross-sectional	General public	3,500	Chronic noncancer pain
Blyth, 2003 [54]	Australia	1998	Cross-sectional	General public	474	Chronic noncancer pain
Braden, 2008 [22]	United States	2000, 2005	Cross-sectional	Database (insurance claims)	1,457,511	Chronic noncancer pain
Breivik, 2006 [73]	Europe Israel	2003	Cross-sectional	General public	4,839	Chronic noncancer pain
Broekmans, 2010 [57]	Belgium	2004–2005	Cross-sectional	Tertiary care	289	Chronic noncancer pain
Buse, 2012 [23]	United States	2004–2009	Longitudinal	General public	5,796	Chronic headache
Calhoun, 2008 [24]	United States	Not reported	Cross-sectional	Secondary care	229	Chronic migraine
Carey, 2009 [25]	United States	2006	Cross-sectional	General public	873	Chronic low back and neck pain
Chen, 2005 [26]	United States	2002–2003	Cross-sectional	Primary care	397	Chronic noncancer pain
Colás, 2004 [76]	Spain	1998–1999	Cross-sectional	General public	74	Chronic headache
Crane, 2015 [27]	United States	2005–2008	Cohort	Database (insurance claims)	30,530	Rheumatoid arthritis Inflammatory polyarthritis
Dureja, 2014 [70]	India	Not reported	Cross-sectional	General public	5,004	Chronic noncancer pain
Eriksen, 2006 [63]	Denmark	2000	Cross-sectional	General public	1,906	Chronic noncancer pain
Fillingim, 2003 [28]	United States	Not reported	Cross-sectional	Tertiary care	240	Chronic low back pain
Fraenkel, 2004 [29]	United States	Not reported	Cross-sectional	Secondary care	100	Osteoarthritis (knee)
Goesling, 2015 [30]	United States	2014	Cross-sectional	Tertiary care	2,104	Chronic noncancer pain
Goode, 2010 [31]	United States	2006	Cross-sectional	General public	141	Chronic low back and neck pain
Gore, 2011 [32]	United States	2008	Cross-sectional	Database (insurance claims)	112,951	Osteoarthritis
Gore, 2012 [10]	United States	2008	Cross-sectional	Database (insurance claims)	101,294	Chronic low back pain
Hanley, 2006 [33]	United States	1997–1998	Cross-sectional	Tertiary care	453	Phantom limb pain
Hansen, 2015 [74]	Norway	2006–2008	Cross-sectional	General public	2,637	Chronic noncancer pain
Hayes, 2018 [34]	United States	2010–2013	Cohort	General public	5,876	Chronic noncancer pain
Hayes, 2018 [35]	United States	2010–2014	Cohort	General public	894	Chronic low back pain
Hoogeboom, 2012 [77]	The Netherlands	2009	Cross-sectional	Primary care Secondary care	401	Osteoarthritis (hip or knee)
Hooten, 2011 [36]	United States	2003–2007	Cohort	Tertiary care	1,241	Chronic noncancer pain
Islami Parkoohi, 2015 [71]	Iran	2012	Cross-sectional	General public	73	Chronic noncancer pain
Jensen, 2006 [64]	Denmark	2000	Cross-sectional	Tertiary care	160	Chronic noncancer pain
Khanna, 2007 [37]	United States	2003	Cross-sectional	Database (insurance claims)	1,157	Rheumatoid arthritis
Kingsbury, 2014 [78]	UK Europe	2011	Cross-sectional	General public	3,750	Osteoarthritis
Knauer, 2010 [38]	United States	2010	Cross-sectional	General public	727	Chronic low back pain
Krymchantowski, 2003 [58]	Brazil	2000–2002	Cohort	Tertiary care	133	Chronic headache
Kung, 2000 [55]	Australia	1993–1996	Cross-sectional	General public Tertiary care	343	Chronic noncancer pain
Kurita, 2012 [65]	Denmark	2010	Cross-sectional	General public	3,305	Chronic noncancer pain
Le, 2012 [39]	United States	2007	Cross-sectional	Database (insurance claims)	258,237	Osteoarthritis
Marschall, 2011 [68]	Germany	2007–2008	Cross-sectional	Database (insurance claims)	19,592	Fibromyalgia

(continued)

Table 1. continued

Author	Country	Sampling Year	Study Design	Setting	No. of Participants	Pain Complaint
Marschall, 2016 [69]	Germany	2012	Cross-sectional	Database (insurance claims)	870,000	Chronic noncancer pain
Miller, 2017 [56]	Australia	2011–2012	Cross-sectional	General public	2,527	Chronic noncancer pain
Moulin, 2002 [79]	Canada	2001	Cross-sectional	General public	2,001	Chronic noncancer pain
Painter, 2013 [40]	United States	2007–2009	Cross-sectional	Database (insurance claims)	245,758	Fibromyalgia
Plesner, 2016 [66]	Denmark	2013	Cross-sectional	Tertiary care	98	Chronic noncancer pain
Poulin, 2016 [59]	Canada	2013	Cross-sectional	Secondary care	58	Chronic noncancer pain
Rahimi-Movaghar, 2004 [72]	Iran	2001	Cross-sectional	Secondary care	309	Chronic noncancer pain
Raval, 2017 [41]	United States	2004–2013	Cross-sectional	General public	6,453	Migraine
Ringwalt, 2014 [42]	United States	2009–2010	Cross-sectional	Database (insurance claims)	81,459	Chronic noncancer pain
Robinson, 2003 [43]	United States	1996–1998	Cross-sectional	Database (insurance claims)	4,699	Fibromyalgia
Schaefer, 2016 [44]	United States	2012	Cohort	Secondary care	347	Fibromyalgia Chronic widespread pain
Shah, 2018 [45]	United States	2011–2015	Cross-sectional	General public	4,921	Osteoarthritis
Sloan, 2019 [47]	United States	2012–2017	Cohort	Database (insurance claims)	93,231	Inflammatory spondylopathies
Shmagel, 2015 [46]	United States	2009–2010	Cross-sectional	General public	700	Chronic low back pain
Suri, 2012 [48]	United States	1990–1991	Cross-sectional	Primary care	855	Chronic low back pain
Toblin, 2011 [49]	United States	2007	Cross-sectional	General public	1,151	Chronic noncancer pain
Torrance, 2007 [61]	England	2004	Cross-sectional	Primary care	1,420	Chronic noncancer pain
Warms, 2002 [50]	United States	1997–1998	Cross-sectional	General public	163	Chronic pain with spinal cord injury
Wasserman, 2014 [51]	United States	2010–2012	Case series	Tertiary care	1,208	Fibromyalgia Chronic noncancer pain
Westergaard, 2015 [67]	Denmark	2010	Cross-sectional	General public	2,087	Chronic headache
Widerstrom-Noga, 2003 [52]	United States	Not reported	Cross-sectional	General public	120	Chronic pain with spinal cord injury
Wolfe, 2013 [53]	United States	2000–2010	Cohort	Secondary care	3,123	Fibromyalgia

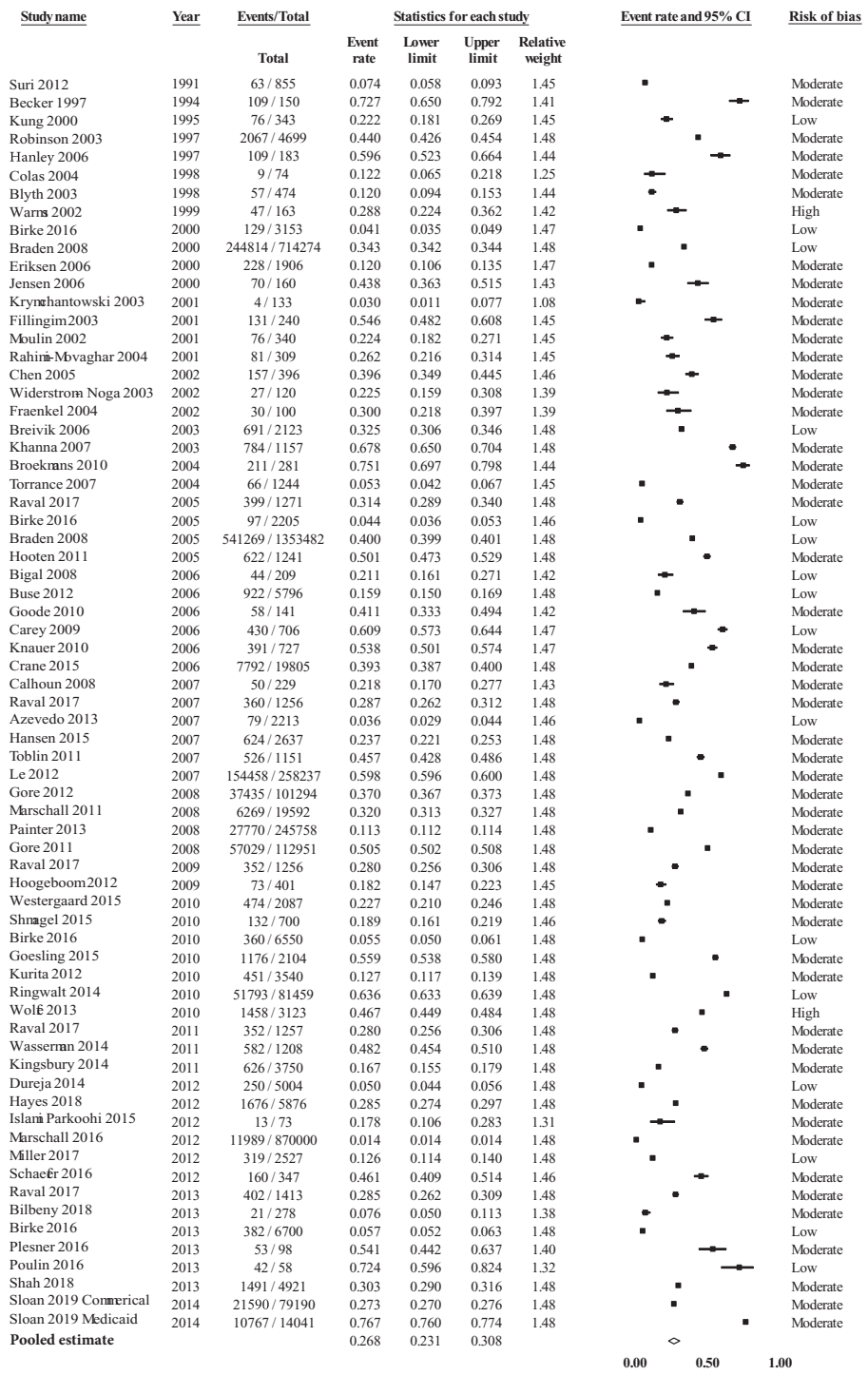

Figure 2. Forest plot of opioid analgesics used by people with chronic noncancer pain. Year represents the midpoint of the sampling period. Data from Sloan et al. [47] represent chronic opioid use of two separate databases of commercial claims (i.e., private insurance) and Medicaid claims.

pain (P=0.091). A model with additional covariates could not be constructed due to the small number of studies.

Sensitivity Analyses

There was little change in estimates of opioid use when the two studies with high risk of bias [50, 53] were removed (26.5%; 95% CI, 22.8–30.6; n=58 studies; low-quality evidence vs 26.8%; 95% CI, 23.1–30.8; n=60 studies; moderate-quality evidence).

When tramadol was classified as a strong opioid, the use of weak opioids increased to 18.9% (14.1% to 24.8%, n=16 studies) and the use of strong opioids increased to 12.0% (9.9% to 14.5%; n=16 studies). There was little change to estimates for use of combination

opioid preparations (a minor decrease in weak combination use to 2.2% [1.6% to 3.1%; n=5 studies] and a small decrease in strong combination use to 4.4% [4.1% to 4.7%; n=2 studies]).

The pooled estimate of opioid use in people with chronic noncancer pain was not affected by the length of time opioids were used. Although studies reported the duration of opioid use from current opioid use to past opioid use, including the last 2 years, these covariates of current and past opioid use were not significant in the meta-regression model (P=0.122).

Discussion

Our review of published studies reporting opioid use in people with chronic noncancer pain found that 26.8% of people with chronic noncancer pain reported using opioid analgesics. In people with chronic noncancer pain, weak opioids were used by more people than strong opioids (17.3% vs 9.8%). In people with chronic low back pain, 29.8% reported using opioids, and strong opioid use was much greater than weak opioid use (28.6% vs 3.1%). We found from meta-regression analysis that geographic region (decreased use in Southeast Asia compared with North America) and setting (tertiary care compared with the general population) significantly contributed to opioid use in people with chronic noncancer pain but that opioid use did not change between 1990 and 2017.

Our review was based on a thorough literature search, summarizing data from 60 studies of over 3.9 million people with chronic noncancer pain reporting on opioid use from 1990 to 2017. We acknowledge that chronic pain diagnoses, as well as opioid use, are often self-reported. The definition of opioid use varied between studies, ranging from current opioid use to opioid use over the last 2 years. However, we accounted for this difference in measurement period during the risk-of-bias assessment (length of prevalence period), and sensitivity analysis confirmed that measurement period did not affect opioid estimates. Despite the number of eligible studies, only 30% of studies reported information on the types of opioids used, and few studies reported on the treatment regimen, so we were unable to determine if there have been changes over time in these aspects of the treatment.

Several covariates were not associated with increased opioid use, including that the use of opioids by people with chronic noncancer pain has not changed over time. This is unexpected and contrary to reports of increasing opioid use in general [8] and reports of the increase in the prescription of opioids to patients with chronic noncancer pain throughout many countries [80–83]. Our previous research found that from 42 studies, the proportion of patients with chronic noncancer pain prescribed opioid analgesics was 30.7% (95% CI, 28.7–32.7), and meta-regression analysis determined that opioid prescribing was associated with year of sampling (more prescribing in recent years; P=0.014) [11]. The explanation for the difference between increasing opioid prescribing and constant self-reported opioid use in people with chronic noncancer pain is unclear but worthy of future exploration.

The proportion of people with chronic noncancer pain in low-income and middle-income countries who use an opioid remains unclear. We found no studies reporting opioid use in low-income countries and only four studies from middle-income countries: three from the upper-middle-income countries of Brazil [58] and Iran [71, 72] and one from a lower-middle-income country of India [70]. The range of opioid use estimates from middle-income countries (3% [58] to 26% [72]) was less than estimates from high-income countries (3% [75] to 72% [62]). This contrasts with the known higher prevalence of chronic pain in low-income and middle-income countries (33% [84]) compared with global estimates (20% [1]). Opioid use in general in low-income and middle-income countries faces several barriers, such as stringent regulations, reduced access to pain medicines, and criminal prosecution [8, 85] that may not be faced as commonly in high-income countries. People with chronic noncancer pain may face similar barriers to accessing opioids.

Similar to clinical practice guidelines for the management of chronic noncancer pain, guidelines for the management of chronic low back pain [86] now discourage the use of opioids for similar reasons of increased risks vs potential benefits [87]. We found that a slightly greater proportion of people with chronic low back pain used opioids compared with the chronic noncancer pain population, but the proportion did not increase over time. The studies reporting opioid use in people with chronic low back pain came from high-income countries; hence, the proportion of people with chronic low back pain from low-income and middle-income countries who use an opioid remains unclear.

Cultural, social, and regulatory differences between countries limit the generalizability of opioid use estimates and the types of opioids used among high-income, middle-income, and low-income countries. Some pharmaceutical companies have identified low-income and middle-income countries as a new source of revenue as "emerging markets." The media have been quick to highlight this social issue [88]. Marketing campaigns have identified countries such as Brazil, with a population of over 200 million, with more than two-thirds of the population affected by chronic noncancer pain [89], as targets to increase opioid sales. This has fueled concern that low-income and middle-income countries may follow in the footsteps of high-income countries with the overprescribing of opioids [90].

Future research may explore the reasons behind the unchanged self-reported use of opioid analgesics in people with chronic noncancer pain over time compared with the increase in the prescription of opioids in this

population over time as previously identified in the literature [11]. Community awareness about the potential harms of opioid analgesics may influence individuals' decisions not to take an opioid medicine they were prescribed, but this has yet to be explored thoroughly in the chronic pain population. The differences between patient and clinician views on opioid use and prescribing have been identified from qualitative research. For example, one study investigating the incentives and barriers to opioid use in acute or chronic musculoskeletal disorders concluded that patients feel that opioids should be used cautiously, whereas clinicians prescribed opioids out of habit and convenience [91]. A recent systematic review of 31 studies identified that people with chronic noncancer pain felt that they were continually balancing the pros and cons of opioids and felt that they were not always "on the same page" as their health care professional [92]. Future studies could examine if opioid prescribing to patients with chronic pain is habitual and if potential contributors such as the increasing prevalence of chronic pain conditions are leading to the increased opioid prescribing for patients with chronic noncancer pain. In due course, future published prevalence studies may identify any changes in the trend of opioid use and/or opioid prescribing following the updated clinical practice guidelines for the management of chronic pain such as those from the Centers for Disease Control and Prevention [6].

Conclusions

Over one-quarter of people with chronic noncancer pain and nearly one-third of people with chronic low back pain report taking opioid analgesics. These proportions did not change during the time period from 1990 to 2017.

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Supplementary Data

Supplementary Data may be found online at http://painmedicine.oxfordjournals.org.

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