Chronic Postoperative Opioid Use: A Systematic Review

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Abstract

Background There are a number of studies in the literature that describe the prevalence, causes, and factors associated with chronic postoperative opioid use, but there is a lack of synthesis of the literature to guide clinicians in optimally managing postoperative pain while avoiding opioid dependence. Thus, the goal of this study was to perform a systematic review of the literature to investigate the prevalence of chronic postoperative opioid use and the associated risk factors.

Materials and methods A systematic search was performed using Ovid Medline and Embase according to PRISMA guidelines. Data were collected on the following outcomes of interest: prevalence of opioid use at 3, 6, and 12 months postoperatively, and risk factors associated with chronic postoperative opioid use.

Results Forty-three articles were included in the final analysis. The mean prevalence of chronic postoperative opioid use in all populations at 3, 6, and 12 months postoperatively was 30.5%, 25.6%, and 25.2%, respectively. The prevalence of patients who developed chronic opioid use at 3, 6, and 12 months postoperatively was 10.4%, 8.5%, and 9.8%, respectively. Forty of the articles analyzed risk factors associated with chronic postoperative opioid use. The most common associated risk factor identified was preoperative opioid use with 27 articles demonstrating a significant association with chronic postoperative opioid use.

Discussion The current opioid crisis is in part secondary to the prevalence of chronic opioid use following surgery. This study identified associated risk factors with chronic postoperative opioid use, which may help identify patients at risk for developing chronic postoperative opioid use.

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A sudden increase in the prescription of opioid medications, combined with a concurrent increase in both opioid-related hospitalizations and deaths, has resulted in an urgent public health problem [1]. The prescription of opioids increased by over 50% in the USA from 2001 to 2010 with an estimated more than 5 million people currently abusing opioids [1]. This has resulted in an increase in opioid-related deaths, with an almost fourfold increase over the recent years translating to approximately 33,000 deaths annually secondary to opioid abuse [2]. While the USA leads the way in the amount of prescription opioids, the increasing number of prescription opioids is a global problem that has also been found in Canada, Austria, and Europe. In 2011, 5% of all patients entering drug treatment programs in Europe reported prescription opioids as their primary drug [3]. The etiology of the opioid crisis is multifactorial. Its origin as a public health crisis can be, in part, traced to the prior recommendations of the American Pain Society and the American Society of Anesthesiologists, which advocated better in-hospital management of pain [4, 5]. The subsequent labeling of pain as a "fifth vital sign" resulted in the marketing of opioids as an equivalent alternative to other, non-addictive, analgesics for the management of moderate pain in both the acute and chronic settings [6–11].

The first opioid exposure that many patients experience is often in the postoperative period, with surgical patients being four times more likely to be discharged with an opioid prescription compared with their nonsurgical counterparts [12, 13]. Surgeons are second only to pain medicine physicians in their rate of prescribing opioids annually [14]. Adequate pain control is a key element in successful recovery after surgery, and inadequate postoperative pain management has been correlated with poor functional recovery; therefore, opioids are often the primary analgesics used in the postoperative period. The recent literature links postoperative opioid use to the subsequent development of opioid dependency [15–18]. In this way, the postoperative period creates a challenging situation of balancing postoperative pain control to optimize recovery, while minimizing the risk of developing chronic use of addictive substances. The current literature pertaining to the use of opioids in the treatment of acute, postoperative pain provides inadequate information [9, 19, 20]. The CDC recommends limiting treatment of acute, postoperative pain with opioids to 7 days [9]. Health Canada recently launched The Opioid Wisely Campaign which included patient resources for the use of opioids in managing postoperative pain [21].

Opioid utilization in the postoperative period is an emerging concern because there is increasing evidence to suggest that patients undergoing surgery are at increased risk of developing chronic opioid use [17, 18, 22]. While the use of opioids for postoperative pain management can be beneficial, chronic use can negatively impact both patients and society [23, 24]. The definition of chronic postoperative opioid use is variable; however, because surgical recovery is expected to occur within 3 months postoperatively, opioid use greater than 3 months postoperatively is generally considered to be chronic. The reasons for the development of postoperative chronic opioid use are complex and multifactorial, and the extent of surgery may not be the only factor that predicts postoperative chronic opioid use. While a number of studies describe the prevalence, causes, and factors associated with chronic opioid use in the postoperative setting, there is lack of synthesis of the literature. Thus, the goal of this study was to perform a systematic review of the literature to identify the common themes associated with chronic postoperative opioid use.

Methods

Search strategy

A systematic search of the literature was performed in April 2018 based on the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. The search aimed to systematically identify all published researches that studied chronic opioid use following surgery. Research databases included Ovid Medline [2000 to April 2018 (week 4)] and Embase. The key terms searched were opioid*, narcotic*, surg*, pain, postoperative, postoperative, perioperative, and perioperative and excluded articles with the key terms palliati*. The symbol "*" denotes all variations of the term beginning with the stem. In addition, reference lists of all studies that underwent full-text reviews were examined to ensure all relevant studies were captured.

Inclusion and exclusion criteria

Two reviewers (J.D. and A.H.) independently reviewed all of the abstracts to identify studies that fulfilled the predetermined eligibility criteria. Title and abstract review were performed once the initial list of studies was generated. Studies were selected if they met the following inclusion criteria: (1) patients treated with opioids in the postoperative setting and (2) the prevalence of opioid use postoperatively was reported for at least one of the following time points: 3, 6, and 12 months postoperatively. A full-text

review was performed on any remaining studies following the title and abstract review. Additional studies that did not meet inclusion criteria were excluded. Any disagreement between the reviewers was resolved by consensus.

Data extraction

Extracted variables included study title, authors, publication year, study design, sample size, and patient demographics including age and gender. We also extracted the surgical procedure, and the prevalence of opioid use at 3, 6, and 12 months postoperatively in both opioid-naïve patients and non-opioid-naïve patients. The definition of chronic postoperative opioid use is variable; however, because surgical recovery is expected to occur within 3 months postoperatively, opioid use greater than 3 months postoperatively is generally considered to be chronic. We also wanted to explore longer use, and because of the variation of the definition of chronic postoperative opioid use, we choose to also look at the proportions of patients using opioids at 6 and 12 months postoperatively. We collected data pertaining to risk factors associated with the development of chronic postoperative opioid use. A comprehensive data collection form based on the outcomes of interest was used for data abstraction. The data were collected by two reviewers (J.D. and A.H.).

Methodologic quality assessment

The quality of the included articles was assessed using the Newcastle–Ottawa Scale (NOS) proposed by Wells et al. [25]. The NOS contains eight items that are given star points if fulfilled, with a minimum score of 1 and a maximum score of 9 stars. The categories covered in the NOS include: (1) selection of the study population, (2) comparability among the groups, (3) outcome or exposure measures for cohort and case–control studies, respectively. A high score is considered 8–9 stars, a medium score is 6–7 stars, and a low score is considered ≤ 5 stars.

Results

Study collection

A total of 8635 articles were identified after the primary literature search (Fig. 1). After title and abstract review, 82 articles met our inclusion criteria for full-text review. Following full-text review, a total of 42 articles were included in the final analysis (Table 1).

Study characteristics

Table 2 summarizes study and clinical characteristics. Thirty-six retrospective cohort studies, six prospective cohort studies, and one case–control study were included in the final analysis. Total cohort numbers for all studies were consistently reported; however, gender and age were inconsistently reported. We reported the demographic information where available. The most common surgery type studied was orthopedic (25 articles) (Table 2). Five articles studied postoperative opioid use in pelvic/abdominal/thoracic procedures. The miscellaneous procedures included: major elective surgery (3 papers), breast (1 paper) and ambulatory surgeries (1 paper), oral cavity surgery (1 paper), and six papers that each studied various procedures.

Methodologic quality

Critique of the methodologic quality of all 43 studies was conducted using the NOS from which the scoring is summarized in Table 1. The majority of articles scored 6 or 7 stars (38 articles) and five articles scored 8 stars.

Synthesis of results

Table 3 lists the proportion of patients with chronic opioid use at 3, 6, and 12 months. Column A lists the proportion of patients with chronic opioid use determined from all the reviewed journal articles when the information was available. Columns B and C list the proportion of chronic opioid use in the "opioid-naïve population" and "non-opioid-naïve population". Articles that did not specify prior opioid use are only reflected in the "All populations' column". The mean prevalence of chronic postoperative opioid use in "All populations" at 3, 6, and 12 months postoperatively was 30.5% (95% CI 23.1–38.0%), 25.6% (95% CI 17.9–33.4%), and 25.3% (95% CI 18.2–32.4%), respectively. Within the opioid-naïve population, the prevalence of postoperative opioid use at 3, 6, and 12 month postoperatively was 10.4% (95% CI 3.1–17/7%), 7.7% (95% CI 0.3–15.2%), and 9.1% (95% CI 3.0–15.2), respectively. The prevalence in non-opioid-naïve patients at 3, 6, and 12 month postoperatively was 54.6% (95% CI 41.1–68.0%), 44.1% (95% CI 30.8–57.3%), and 48.5% (95% CI 33.8–63.1%), respectively.

Forty of the articles examined risk factors associated with chronic postoperative opioid use (Table 4). Pooled analysis was not possible secondary to the heterogeneity of the studies. The most common risk factor found (27 articles) was preoperative opioid use. The definition of what constituted preoperative opioid use was inconsistent. Six of the articles defined preoperative opioid use as any opioid

Table 1 Summary of results and quality assessment of included studies

Study	Study design	Patients (n)	Type of surgery	Proportion of patients with chronic opioid use postoperatively (%)									Quality assessment Total
				Opioid-naïve			Prior opioid user			Opioid not specified			
				3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months	
Ahn et al. [36]	Retrospective	195	Orthopedic							18			8
Al Dabbagh et al. [37]	Retrospective	861	Orthopedic		45	36							8
Alam et al. [18]	Retrospective	391,139	Miscellaneous			7.7							7
Anderson et al. [38]	Retrospective	1002	Orthopedic			18.6			38.8				7
Anthony et al. [39]	Retrospective	4946	Orthopedic							7.24		4.71	7
Armaghani et al. [27]	Prospective	583	Orthopedic			26			59			44	7
Bateman et al. [40]	Retrospective	80,127	Pelvic/abdominal/thoracic		0.2	0.3							7
Bedard et al. [41]	Retrospective	4205	Pelvic/abdominal/thoracic	6.46	3.17	3.75	35.76	28.05	25.62	14.2	10.4	9.8	7
Bedard et al. [42]	Retrospective	73,959	Orthopedic	10.2	4	2.2	50.4	38.3	33.2	24.9	16.3	14.6	7
Brat et al. [43]	Retrospective	1,015,116	Miscellaneous			0.2							7
Brummett et al. [30]	Retrospective	36,177	Miscellaneous	6									8
Carroll et al. [28]	Prospective	109	Miscellaneous								6		7
Clarke et al. [17]	Retrospective	39,140	Miscellaneous	3.1									7
Connolly et al. [44]	Retrospective	8377	Orthopedic							50	40	29.3	7
Deyo et al. [45]	Retrospective	2491	Orthopedic		3.6			32.4			43.9		7
Goesling et al. [46]	Prospective	574	Orthopedic		6.0		41.7	41.7					7
Hansen et al. [47]	Retrospective	15,020	Orthopedic	0.7			66.5			5.2			7
Hernandez et al. [48]	Retrospective	105	Orthopedic			0.95							7
Holman et al. [49]	Retrospective	613	Orthopedic	12			20			19.7			8

Table 1 continued

Study	Study design	Patients (n)	Type of surgery	Proportion of patients with chronic opioid use postoperatively (%)									Quality assessment
				Opioid-naïve			Prior opioid user			Opioid not specified			Total
				3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months	
Huang et al. [50]	Prospective	200	Miscellaneous							9.5			7
Inacio et al. [15]	Retrospective	9525	Orthopedic	2.1						5.2			7
Johnson et al. [51]	Retrospective	77,573	Orthopedic	10.0									7
Kim et al. [52]	Retrospective	57,545	Orthopedic									7.6	7
Kulshrestha et al. [53]	Retrospective	1045	Pelvic/ abdominal/ thoracic							16.8		14.6	7
Mahowald et al. [54]	Retrospective	413	Orthopedic		2.9					36	30		7
Marcusa et al. [55]	Retrospective	4113	Miscellaneous	10									7
Massey et al. [56]	Retrospective	50	Orthopedic		7.1			52.8					7
Mudumbai et al. [29]	Retrospective	64,391	Miscellaneous	13.7	8	3.5	86.5	80.5	70.2				7
Namba et al. [57]	Retrospective	23,726	Orthopedic							92.7	42.1	30.4	7
Pang et al. [58]	Retrospective	99	Miscellaneous	67.5			23.7			41			6
Politzer et al. [59]	Retrospective	66,950	Orthopedic		5			34.8					7
Raebel et al. [22]	Retrospective	10,643	Pelvic/ abdominal/ thoracic	4									7
Raebel et al. [60]	Retrospective	11,719	Pelvic/ abdominal/ thoracic				77						7
Rosenbloom et al. [61]	Prospective	122	Orthopedic							35.25			7
Rozet et al. [62]	Retrospective	145	Orthopedic	8			80			30			7
Schoenfeld et al. [63]	Retrospective	9991	Orthopedic	1	0.1	0.02							7
Soneji et al. [64]	Retrospective	39,140	Miscellaneous			0.4							7

Table 1 continued

Study	Study design	Patients (n)	Type of surgery	Proportion of patients with chronic opioid use postoperatively (%)									Quality assessment
				Opioid-naïve			Prior opioid user			Opioid not specified			Total
				3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months	
Stark et al. [65]	Prospective	970	Miscellaneous	10.5									7
Sun et al. [66]	Retrospective	120,080	Orthopedic	1.80			67.72						8
Sun et al. [67]	Retrospective	641,941	Miscellaneous			5.426							7
Westermann et al. [68]	Retrospective	35,155	Orthopedic							19.20	12.50	9.65	7
Zarling et al. [69]	Retrospective	315	Orthopedic			22			64				7

use within 3 months prior to surgery, whereas 12 studies defined preoperative opioid use as use for greater than 3 months prior to surgery; the remaining studies did not clearly define preoperative opioid use. Other common risk factors identified included prior psychiatric diagnosis (22 articles), substance (illicit drugs) abuse (11 articles), alcohol abuse (8 articles), and tobacco smoking history (8 articles). Females compared to males were often identified to be at higher risk of developing chronic postoperative opioid use (9 vs. 2 articles, respectively). Younger age was also a common risk factor identified although the definition of "younger" age was inconsistent (15 articles). The presence of comorbidities was also determined to be a predictor of chronic postoperative opioid (16 articles).

Discussion

In this systematic literature review, we found that chronic postoperative opioid use is most likely to occur in patients with a history of opioid use prior to surgery. Furthermore,
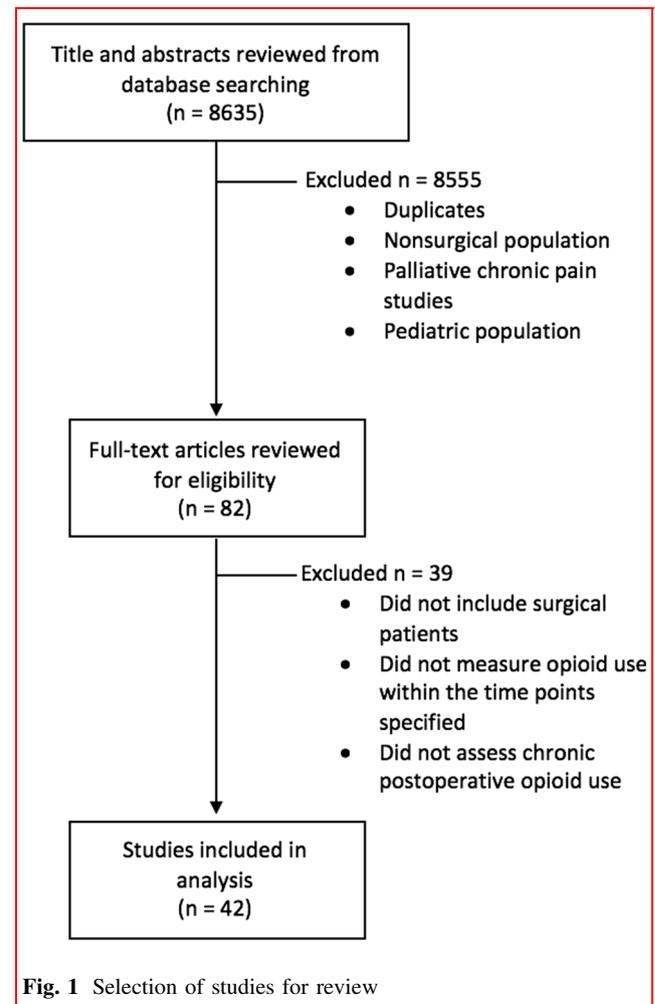

Fig. 1 Selection of studies for review

Table 2 Characteristics of included studies

Characteristic	Total
Study design	
Retrospective cohort	35
Prospective cohort	6
Case–control	1
Total patients	2,851,809
Gender	
Female	1,631,355
Male	1,055,022
Age	
Mean age	58.52
Minimum age	18
Maximum age	103
Surgical procedures	43
Orthopedic	25
Limb	21
Axial	5
Pelvic/abdominal/thoracic	5
Open	3
Laparoscopic	2
Miscellaneous	12

Table 4 Total number of papers identifying specific risk factors

Risk factor	Number of articles
Prior opioid use	27
Psychiatric history	22
Comorbidities	16
Younger age	15
Substance abuse	11
Tobacco smoking	9
Female gender	9
Alcohol abuse	8

other factors such as a psychiatric history, drug and alcohol abuse, female sex, and young age were more commonly associated with chronic postoperative opioid use. Importantly, our review also found up to 10% of patients with no prior history of opioid use become chronically dependent after surgery.

We believe the current opioid crisis is in part secondary to the prevalence of chronic opioid use following surgery. This systematic review demonstrated that there is a broad range of reported chronic postoperative opioid prevalence. The reasons for the wide range of reported chronic opioid use is multifactorial. Some of the reasons we identified include: inconsistent definitions of pre- and postoperative opioid use, heterogeneity of the articles with respect to surgeries and patient populations studied, and a varying

quality of the papers reviewed. At one extreme, Schoenfeld et al. reported a prevalence of 0.02% of spinal surgery patients using opioids 12 months postoperatively compared to 70.2% of surgical patients reported by Mudumbai et al. However, Schoenfeld reported this prevalence in the setting of opioid-naïve patients, whereas Mudumbai studied patients with prior opioid use.

The most common and consistent theme identified in this review was the association between preoperative opioid use and chronic postoperative use. Twenty-seven papers in our review studied the prevalence of preoperative opioid use and its association with chronic postoperative opioid use, and all papers demonstrated a significant relationship. The studies, however, failed to describe or identify those patients who underwent surgery to eliminate the pain that was the reason for their preoperative opioid use. A patient undergoing a surgical procedure that is not related to the indication for the preoperative use of opioids would not be expected to eliminate their opioid use, and this was not captured in the articles analyzed in this review. The inconsistent definition of preoperative opioid use could partially account for the wide range of postoperative opioid use reported in the non-opioid-naïve population (Table 3). Preoperative opioid use and its association with chronic postoperative opioid use is likely multifactorial. Preoperative opioid use can lead to tolerance and hyperalgesia, which can make acute postoperative pain difficult to control and lead to higher opioid demand and chronic use [26].

Table 3 Proportion of patients with chronic postoperative opioid use

	All populations			Opioid-naïve population			Non-opioid-naïve population		
	3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months
Average	30.5	25.6	25.3	10.4	7.7	9.1	54.6	44.1	48.5
Minimum	0.7	0.1	0.02	0.7	0.1	0.02	20.0	28.1	25.6
Maximum	92.7	80.5	70.2	67.5	45.0	36.0	86.5	80.5	70.2

All numbers are percentages

Armaghanni et al. demonstrated that preoperative opioid use was also associated with higher opioid demand in the immediate postoperative period and higher rates of opioid use 12 months postoperatively (59% vs. 26% in the opioid-naïve population) [27]. Carroll et al., while controlling for preoperative opioid use, determined the time for patients to return to their preoperative opioid dosage and compared that with the time to cessation in the opioid-naïve population. Patients taking opioids preoperatively took longer to return to their preoperative dosage compared to the opioid-naïve patients [28].

The presence of a psychiatric diagnosis prior to surgery also strongly predicted chronic postoperative opioid use. Twenty-two studies found that a prior psychiatric diagnosis was significantly associated with chronic postoperative opioid use. In both the opioid-naïve and non-opioid-naïve populations, a psychiatric diagnosis—predominantly anxiety and/or depression—was strongly associated with a risk of chronic opioid use postoperatively. Pain, therefore, is not the only contributing factor for chronic postoperative opioid use and a psychiatric illness may be a predisposing factor.

This review demonstrated orthopedic surgery is associated with a high prevalence of chronic opioid use; however, there is a strong selection bias in the literature towards postoperative opioid use and orthopedic surgeries which is unsurprising given that orthopedics is the third highest opioid-prescribing specialty [12]. Of the 43 studies analyzed in this review, 26 investigated opioid use in the setting of orthopedic procedures. However, the other surgical specialties reporting chronic postoperative opioid use showed similar findings to the orthopedic population. We therefore believe the results of our study are generalizable to broader surgical populations. The current available data are insufficient to determine which surgical procedures present the highest risk of chronic postoperative opioid use. To assume that a higher degree of postoperative pain predicts a higher risk of developing postoperative chronic opioid use is not supported by our review. Mudumbai et al. studied a variety of surgical procedures and reported that prior opioid use was the best predictor of postoperative opioid use independent of surgical procedure [29]. Importantly, Brummett et al. compared the incidence of new chronic opioid use in patients undergoing major versus minor surgical procedures and found the incidence of chronic postoperative opioid use did not differ between major and minor surgical procedures [30]. Carroll et al. demonstrated that pain duration and intensity were not predictive of postoperative opioid duration [28]. Chronic postoperative opioid use is, therefore, not entirely due to the surgical extent or postoperative pain intensity. Further research should investigate other surgical procedures, such as oncologic surgery, that may be at high risk of developing chronic postoperative opioid use.

Managing postoperative pain remains a challenge for surgeons, and adequate pain control must minimize the risk of opioid-related adverse events, including chronic use. Adequate control of postsurgical pain is a vital part of optimizing a patient's postoperative recovery. While opioids continue to be a primary analgesic used for controlling moderate-to-severe postoperative pain, clinicians need to be aware of the risks of over-prescribing opioids and employ alternative strategies to mitigate these risks [31]. One such strategy is the use of multimodal analgesia, which has been shown to be effective in controlling postoperative pain and can help reduce the use of opioids and the subsequent development of chronic postoperative opioid use [32, 33]. The CDC recommends limiting treatment of acute, postoperative pain with opioids to 7 days [9]. Hartford et al. recently demonstrated that the implementation of a standardized pain care bundle decreased opioid prescriptions and use while still effectively controlling patients' pain through the use of multimodal analgesia. This study demonstrated the importance in tracking surgeons' opioid-prescribing habits while implementing a protocol for postoperative opioid prescriptions in line with the CDC recommendations of limiting opioid use to within the first 7 days postoperatively [34].

Limitations

This systematic review was conducted to improve our understanding of the role of surgery in contributing to the current opioid epidemic. A formal meta-analysis could not be conducted because of study heterogeneity and the lack of outcomes amenable to pooling of data. There is a strong selection bias toward orthopedic procedures, possibly making the findings less generalizable to broad surgical populations. However, other surgical specialties were represented in this literature review, with similar findings to the orthopedic population. We therefore believe our findings are relevant to other surgical populations. This study is also limited by the endpoint of use or non-use of opioids at the specified time points. Due to the data presented in the literature, we were unable to describe the population of patients who undergo surgery and as such continue to use opioids, however, at a much significant lower amount and dose compared with preoperative opioid use. Lower-quality papers, not reflected by the NOS score, may have been included in this review because they met the inclusion criteria and may have additionally contributed to the wide variation in reported proportions of patients with chronic postoperative opioid use. Although a recent systematic review recommended the use of NOS when assessing the risk of bias and methodologic quality of observational

studies, such as case–control or cohort design, NOS has been shown to perform better for case–control studies compared to cohort studies. The majority of studies reviewed were retrospective cohort studies (36 studies) with only one case–control study included [35].

Conclusion

Finally, although there was wide variation in the reported proportions of patients using chronic opioids postoperatively, we believe the averages are realistic approximations of the truth. Further research needs to be performed to better understand high-risk surgical procedures outside of orthopedic surgery. We identified associated risk factors and chronic postoperative use. Although we cannot say these associated factors have a causal relationship with chronic postoperative opioid use, we believe this information will help clinicians become more aware of patients at a potentially higher risk of continued opioid use postoperatively. With this information, we hope clinicians will consider implementing strategies to help reduce perioperative and chronic postoperative opioid use.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict on interest.

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