Effectiveness of organisational interventions on the appropriate use of opioids for non-cancer pain upon hospital discharge: A systematic review

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Abstract

Aim: To summarise the effectiveness of organisational interventions on appropriate opioid use for non-cancer pain upon hospital discharge. Methods: A systematic search was conducted on six electronic databases by two independent reviewers. We included original research articles reporting on quantitative outcomes of organisational interventions targeting appropriate opioid use on hospital discharge. Quality assessment was performed by two independent reviewers. The protocol for this review was prospectively registered on PROSPERO (ID: CRD42020156104). Results: Out of 173 full texts assessed for eligibility, 43 were included in this review. The majority of studies had a moderate to serious risk of bias (33 out of 43). Most of the studies implemented a multifaceted organisational intervention (16 studies). Other interventions included guideline implementation, prescriber education and default opioid prescribing quantity changes in electronic medical records. Multiple studies found that the dissemination of patient-specific and procedure-specific guidelines reduced the quantity of opioids prescribed by 44-57%. Prescriber education provided with feedback was implemented in four studies and resulted in a 33-44% decrease in prescribing rates. Lowering the default quantities in the electronic medical records produced a 40% decrease in opioids prescribed in one study. Conclusion: Guideline implementation, prescriber education and default opioid prescribing quantity changes all appear effective in improving the appropriate use of opioids on hospital discharge. However, the extent of reduction of opioid prescribing upon hospital discharge after the implementation of multifaceted intervention strategies appears similar to that of simpler interventions which require fewer resources.

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ABSTRACT

Aim : To summarise the effectiveness of organisational interventions on appropriate opioid use for non-cancer pain upon hospital discharge.

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Results : Out of 173 full texts assessed for eligibility, 43 were included in this review. The majority of studies had a moderate to serious risk of bias (33 out of 43). Most of the studies implemented a multifaceted organisational intervention (16 studies). Other interventions included guideline implementation, prescriber education and default opioid prescribing quantity changes in electronic medical records. Multiple studies found that the dissemination of patient-specific and procedure-specific guidelines reduced the quantity of opioids prescribed by 44-57%. Prescriber education provided with feedback was implemented in four studies and resulted in a 33-44% decrease in prescribing rates. Lowering the default quantities in the electronic medical records produced a 40% decrease in opioids prescribed in one study.

Conclusion : Guideline implementation, prescriber education and default opioid prescribing quantity changes all appear effective in improving the appropriate use of opioids on hospital discharge. However, the extent of reduction of opioid prescribing upon hospital discharge after the implementation of multifaceted intervention strategies appears similar to that of simpler interventions which require fewer resources.

Keywords : discharge, hospital, interventions, opioid

What is already known about this subject

Harms related to the use of opioid analgesics after discharge from hospital is well established.

Previous systematic reviews have examined the effectiveness of interventions in improving the appropriate use of opioids for surgical patients on hospital discharge and for patients discharged from the emergency department.

What this study adds

Interventions involving guideline implementation, prescriber education and default opioid prescribing quantity changes all appear effective in improving the appropriate use of opioids on hospital discharge.

Multifaceted intervention strategies offered no additional improvements in opioid prescribing compared to single intervention strategies.

1 INTRODUCTION

Opioid analgesics are often prescribed on hospital discharge for the continued management of moderate to severe acute pain.[1] However, opioids are often prescribed in excess, with up to 92% of patients reporting unused opioids after surgery as found in a systematic review conducted in 2017.[2] Excessive discharge opioid prescribing contributes towards an opioid reservoir in the community and poses a health risk due to the potential for diversion, misuse or overdose.[3,4] Additionally, patients prescribed opioids on hospital discharge are more likely to use opioids long term when compared to those not given opioids.[5] A systematic review

of 28 studies conducted in 2020 showed that 10.4% of opioid-naïve patients prescribed opioids on hospital discharge were still using opioids three months after hospital discharge.[5] Such long-term opioid use increases the potential for harm including dependence, tolerance, and even death.[6]

Increasing attention to harms associated with inappropriate opioid prescribing has led to numerous efforts to enhance the safe use of opioids.[7] A systematic review on the impact of interventions to improve opioid use upon surgical discharge reported that clinician-mediated strategies such as prescribing guidelines and education, as well as organisational strategies such as shared decision-making were effective in improving appropriate opioid use.[4] A systematic review evaluating the effectiveness of interventions on appropriate opioid use upon discharge from the emergency department (ED) found that education and guideline interventions were effective in decreasing prescribing rate.[8] However, to our knowledge, no review has examined and summarised the effectiveness of opioid prescribing interventions among all patients upon hospital discharge.[1,3,4] Thus, our review aims to examine the effectiveness of organisational interventions on appropriate opioid use for non-cancer pain upon hospital discharge.

2 METHODS

The review was performed in accordance with the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)*guidelines.[9] The protocol for this review was prospectively registered on the *International Prospective Register of Systematic Reviews (PROSPERO* , ID: CRD42020156104).

2.1 Inclusion and exclusion criteria

The inclusion criteria included original research articles published during the last 10 years. The 10-year range was implemented due to opioid overdose deaths increasing rapidly after 2010.[10] We included articles which reported quantitative outcomes of organisational interventions targeting the appropriate use of opioids for non-cancer pain upon hospital discharge. Organisational interventions were defined as initiatives designed and implemented by each hospital and included clinician-mediated strategies. The appropriate use of opioids, as defined by the studies, may be measured by changes in prescribing (e.g. proportion of patients discharged with an opioid and amount of opioids prescribed) or clinical outcomes (e.g. pain intensity and side effects). Hospital discharge included admitted patients being discharged from hospital inpatient care or the ED.

The exclusion criteria included opioid use for palliative care, oncology/cancer pain or opioid-substitution therapy. Interventions primarily involving state laws and mandates were excluded as they were outside the scope of this review. Studies involving participants aged below 18 years; case reports or case series, conference abstracts, expert opinion articles, literature reviews; and studies written in languages other than English were excluded.

2.2 Search Strategy

A comprehensive search strategy was developed in consultation with an academic liaison librarian. It used a combination of subject headings and keywords around the following themes: opioid analgesics, organisational interventions to change prescribing practices and medications prescribed upon hospital discharge. The subject headings and keywords were modified with appropriate syntax relevant to each database and the full search strategy is available in Appendix 1.

Searches were performed on 6 electronic databases: MEDLINE (2011 – Present), Scopus (2011 – Present), Embase (2011 – Present), Cochrane Central Register of Controlled Trials (2011 – Present), International Pharmaceutical Abstracts (2011 – Present) and PsycINFO (2011 – Present). The last search was run on 23 March 2021.

Reference lists of included studies were also screened to identify any additional relevant studies.

2.3 Data extraction

After removing duplicates, two independent reviewers (SL and KP) screened the articles by title and abstract and assessed them for eligibility. The full texts of articles that were considered possibly relevant were then

assessed for eligibility. Any discrepancies were discussed with a third reviewer (JP) until consensus was made.

Information on the author, country and year of the study conducted, study size, design and duration, intervention performed, opioid-related and clinical outcomes were extracted and summarised in tables. If any results were unclear or missing, the corresponding author was contacted and asked to provide relevant information.

2.4 Quality assessment

Two independent authors (SL and KP) assessed the quality of each study using *Risk of Bias 2 (RoB2): A revised Cochrane risk-of-bias tool for randomised trials*[11] and the *Risk Of Bias In Non-randomised Studies of Interventions*[12] tool for non-randomised studies (Appendices 2 and 3). Any discrepancies were discussed with a third reviewer (JP) until agreement was reached. Visual representations of the risk of bias assessments were produced using the*Risk-of-bias VISualization (robvis)* tool to provide a summary (Appendices 4 and 5).[13]

2.5 Data synthesis

Studies were grouped by the following intervention types: guideline or protocol implementation, changed default quantities in electronic medical records, and educational interventions. Any study that employed more than one of these interventions was classed as a multifaceted intervention.

3 RESULTS

The comprehensive search produced a total of 6,785 articles, of which 173 full texts were assessed for eligibility. Upon further refinement using the inclusion and exclusion criteria, a total of 43 texts were included (Figure 1). The results from these studies are summarised in tables 1-4.

3.1 Study characteristics

Of the 43 articles included in this review, there were three randomised controlled trials (RCTs),[14-16] four cohort studies,[17-20] one case-control study[21] and 35 pre-post intervention/interrupted time series studies.[22-56]

Nineteen studies involved patients discharged from the ED,[15,16,22-24,26-29,31,34,39-42,46,48,50,56] four focused on women recovering from caesarean delivery,[18,25,32,45] eight looked at all surgical patients,[14,20,33,35,42,52-54] and four involved all discharge patients.[38,42,55,56] The remaining studies focused on more specialised surgical procedures including endocrine, orthopaedic and cardiac surgery.

The studies included were conducted in the United States of America (n=34),[15-28,30-33,35-41,43-45,47-50,55,56] Australia (n=8)[14,29,34,42,51-54] and the United Kingdom (n=1).[46]

There were 16 studies which employed a multifaceted intervention,[16,18,24,25,31,37,38,42,45,46,49,50-52,54,55]13 studies implemented guidelines or protocols to guide prescribing,[17,21,23,27,30,32,36,40,41,43,44,47,53] 11 studies used educational interventions[14,15,19,20,22,26,28,29,33-35] and three studies changed the default quantities of discharge opioids in the electronic medical records.[39,48,56]

The predominant prescribing outcomes reported were changes in the quantity of opioids prescribed or changes in the proportion of patients discharged with an opioid prescription. Four studies reported clinical outcomes which included changes in pain intensity following discharge or the number of returns to the ED with uncontrolled pain.

3.2.1 Multifaceted interventions aimed at prescribing

Sixteen studies implemented multiple intervention strategies to improve prescribing on hospital discharge.[16,18,24,25,31,37,38,42,45,46,49,50-52,54,55]The majority of these studies included health professional education in conjunction with other interventions.

Eight studies provided education on appropriate opioid prescribing as well as guidelines and decision-making tools to support prescribing.[18,24,31,37,38,51,52,55] A retrospective cohort study by Landau et al. provided a

protocol for opioid prescribing focusing on a stepwise approach to multimodal analgesia.[18] This intervention resulted in a relative increase of 93% in the number of oxycodone-free prescriptions. A prospective pre-post study conducted in 2018 by Meisenberg et al. implemented prescriber education, tools to guide opioid prescribing, reduction of the default standard prescription order, patient education and public education about opioid risks. They showed a relative decrease in the amount of opioids prescribed per encounter by 58%. This was not accompanied by an increase in return visits to ED post-intervention, highlighting that clinical outcomes were not adversely impacted by reducing the amount of opioids prescribed on discharge.[38]

Two pre-post studies[38,52] and one interrupted time series[24] provided feedback after the education sessions and implemented guidelines. These studies showed a relative decrease in opioid prescribing per patient of 28-58%[24,38] and total inappropriate opioid prescribing by 37%.[52]

Four studies involved modifications to the prescribing workflow or environmental remodelling in addition to prescriber education.[25,46,50,54] A retrospective pre-post study by Raman et al. involved a two-phase intervention, with education provided in the first phase and a stock reduction of paracetamol/codeine tablets in phase two.[46] The education session resulted in a relative decrease in the amount of opioids prescribed by 59%, but the reduction in stock kept by the pharmacy had no effect on prescribing patterns. A retrospective pre-post study by Tran et al. used pharmacist-assisted prescribing for opioid prescriptions.[54] The pharmacist would discuss discharge medications with the patient, prepare and print the prescriptions, and then discuss the medications with the hospital doctor. This resulted in a relative decrease in the amount of oxycodone prescribed by 50%.

A prospective pre-post study by Prabhu et al. implemented discussions with the patient about their analgesia in addition to decreasing the maximum opioid prescription quantity to 25 tablets in the departmental protocol.[45] The quantity of opioids prescribed was decided by shared-decision making with the patient after counselling them on the risks and correct use of opioid analgesia. This intervention resulted in a relative decrease of 20% in the number of opioid tablets prescribed.

3.2.2 Guidelines and protocols implemented to guide prescribing

Thirteen studies assessed the implementation of protocols and guidelines in guiding opioid prescribing upon hospital discharge.[17,21,23,27,30,32,36,40,41,43,44,47,53] These guidelines included recommendations for multimodal analgesia, procedure-specific prescribing, patient-specific prescribing, and general guidelines.

Five studies employed multimodal analgesia guidelines using paracetamol, gabapentin, naproxen and celecoxib as first-line choices for pain management.[17,21,30,41,53] If pain was uncontrolled, patients were provided with either 10-20 tablets of tramadol, oxycodone or paracetamol with codeine combination, or up to 7-days supply of hydrocodone. These studies found a relative decrease of 36-93% in the proportion of patients discharged with an opioid, and a relative decrease of 26% in the quantity of opioids prescribed per patient discharge.

Two studies focused on implementing procedure-specific guidelines, where the expected pain from the procedure guided the amount of opioids prescribed on discharge.[36,47] These guidelines were both effective in improving the appropriate use of opioids with a prospective pre-post study by Linder et al. reporting a relative decrease in the quantity of opioids prescribed by 44%[36] and a retrospective pre-post study by Sada et al. reporting a relative decrease in the proportion of patients discharged with an opioid by 20%.[47]

Three studies used the amount of opioids consumed during the 24-48 hours prior to discharge to guide prescription quantities.[32,43,44] All of these pre-post studies showed a relative reduction in both the proportion of patients discharged with an opioid (56% decrease), and the amount of opioids prescribed (31-56% decrease).

Three studies implemented general prescribing guidelines.[23,27,40] They were less prescriptive than the other types of guidelines previously mentioned and their recommendations included avoiding prescribing extended-release opioids and limiting the number of opioid tablets provided on discharge. These found a relative decrease in the proportion of patients given opioids on discharge of 16-36% and a relative decrease in the number of opioid tablets per prescription of 15%.

3.2.3 Educational interventions aimed at prescribing

Eleven studies employed educational interventions to improve prescribing.[14,15,19,20,22,26,28,29,33-35] These interventions included lectures, audit and feedback and the distribution of pocket cards. A RCT conducted by Michael et al. explored the effect of audit and feedback by providing prescribers with their opioid prescribing data in comparison to their peers.[15] This method had both short-term and long-term effects in decreasing the proportion of patients discharged with an opioid prescription, with a relative reduction of 39% at six months, and 47% at 12 months.

Three studies employed multiple educational interventions simultaneously including education sessions, information emails, pharmacist-led discussions and pocket cards.[19,34,35] A cohort study by Oyler et al. showed a relative decrease of 50% in the median amount of opioids prescribed per day after implementing multiple educational strategies.[19]

Four studies provided a single educational intervention and these produced mixed results.[14,20,29,33] A RCT by Hopkins et al. provided a single 30 minute face-to-face educational session, and this resulted in a relative decrease of 20% in the quantity of opioids prescribed on discharge. One retrospective pre-post study provided training on a morphine equivalent daily dosing calculator in the electronic medical record and did not report a statistically significant change.[33]

3.2.4 Changes to default quantities in electronic medical records

Three retrospective pre-post studies explored the effect of changes to default quantities in electronic medical records.[39,48,56] Two of the studies did not set default quantities after removal of the autopopulation function.[48,56] This function set a specific number of opioid tablets upon selection of an opioid in the electronic medical record. The studies that removed this function produced mixed results in opioid prescribing patterns, with one pre-post study showing a relative decrease in the quantity of opioid tablets prescribed of 25%,[48] and another pre-post study showing no significant change in quantity prescribed.[56] A pre-post study by Montoy et al. removed the autopopulation function and then set lower quantities for commonly prescribed opioids including oxycodone and combination products of oxycodone/paracetamol and hydrocodone/paracetamol.[39] When the default quantity was reduced from 20 to five tablets, there was a 40% relative decrease in the quantity of opioid tablets provided on discharge.

3.3 Quality assessment

A risk of bias assessment was performed for three RCT's and 40 non-randomised studies. A moderate or serious risk of bias was found for 30 studies, and this was predominantly due to the bias introduced by confounding factors or methods of measuring outcomes.[17-23,25-41,43,46-50,52,53]

4 DISCUSSION

This review identified that procedure-specific, patient-specific and multimodal analgesia guidelines, as well as educational interventions and lowering default opioid prescription quantities produced the greatest reduction in opioid use. However, most studies were of moderate to high risk of bias and did not investigate whether reducing discharge opioid prescribing impacted clinical outcomes. Although implementation of multifaceted interventions also demonstrated a significant decrease in the amount of opioids prescribed on discharge, the extent of this reduction appears similar to results produced by simpler interventions which require fewer resources. In particular, guideline-based interventions and changes to default discharge opioid quantities in electronic medical records may be the most cost-effective as they require the least amount of time and resources to implement.

Our study found that the implementation of patient-specific and procedure-specific guidelines were as effective as multimodal analgesia guidelines in improving appropriate opioid use on hospital discharge. These results add to the findings identified in the systematic reviews conducted by Wetzel et al. (2018) and Daoust et al. (2022) exploring the effect of interventions on discharge opioid prescribing after surgery[4] and from ED respectively.[8] Wetzel at al. (2018) found that implementation of multimodal analgesia guidelines, as well

as the education of prescribers and patients were effective in decreasing the total number of opioid tablets prescribed on discharge. Daoust et al (2022) identified that prescriber feedback, education and guideline implementation were effective interventions in improving the appropriate use of opioids on discharge from the ED. Our review included an additional 30 articles that were not included in the previous reviews, and found that implementing interventions for specific procedures and specific departments of the hospital, such as specialty surgical units or the emergency department, may be more effective than whole hospital approaches and just as effective as multimodal analgesia guidelines.

Out of the 43 studies included in this review, there were six studies that showed no significant improvement in opioid prescribing after intervention implementation.[20,41,49,53,55,56]Generally, these studies found a lower MME provided on discharge pre-intervention than similar studies that found an improvement in opioid prescribing. In their study investigating the effect of guideline implementation on the mean MME per discharge prescription, Pace et al. found no significant decrease from a pre-intervention MME of 132 to 106 MME's post-intervention.[41] In similar studies by Linder et al. and Peterman et al., a significant decrease in opioid prescribing was found after guideline implementation from a pre-intervention MME of 200 and 225 respectively.[36,44]This suggests that interventions could be more effective when there is a higher rate of pre-intervention opioid use upon hospital discharge.

Despite the evidence that providing written information to patients aids in improving adherence to therapy, there has been limited research to evaluate the effects of interventions on improving provision of an analgesic discharge plan.[57] Only a few studies included in this review mentioned weaning plans,[20,51,52] and only one study explored how interventions improved the provision of an analgesic discharge plan upon hospital discharge.[51] In their study, Stanley et al. found that the provision of an opioid weaning plan increased from 7% to 87% of patients after guideline implementation, education and the development of an expert advisory group to oversee the intervention.[51] Further research is required to evaluate the effect of different intervention types on discharge plan provision, as well as evaluating the effect of such a plan on opioid use following hospital discharge.

The main strength of this review was the systematic search conducted to identify relevant articles. A comprehensive search strategy was produced in consultation with a clinical librarian and was applied to six databases, thus identifying a broad range of relevant literature. Two independent authors assessed the eligibility of articles retrieved from the search and assessed the quality of all included articles.

However, there are some limitations to our review. Firstly, a meta-analysis could not be performed due to the large degree of heterogeneity in interventions implemented and outcomes reported. There was also a large degree of heterogeneity between the reporting of opioid quantities in the studies. This meant that conversion of quantities to a common unit such as MME's was not possible, meaning that greater comparability was not achievable. As the focus of our review was on organisational interventions, we did not assess the effectiveness of other intervention types such as state laws and mandates on opioid prescribing upon hospital discharge. Furthermore, some relevant articles may have been missed, as we omitted any articles not written in English and did not search grey literature. Also, the time period for our search was limited to 10 years, thus not allowing for an evaluation of changes in intervention efficacy over time or research published prior to this. Finally, the follow-up period for the majority of studies in this review was less than 24 months, thus the long-term sustainability of these interventions is unknown.

5 CONCLUSION

Interventions focusing on guideline dissemination, prescriber education and changes to default opioid prescription quantities appear effective in improving the appropriate use of opioids prescribed upon hospital discharge. Lower cost is involved in the implementation of guidelines and changing default opioid prescription quantity. Future studies should assess changes in clinical outcomes accompanying changes in discharge opioid prescribing.

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STATEMENT OF ORIGINALITY

This work is submitted for publication in the British Journal of Clinical Pharmacology. The authors declare that this work has not been, and, if accepted for publication, will not be published in part or in full in any other journal. All authors have read and approved the final manuscript in its submitted form.

CONTRIBUTORS

JP and SL conceived the study and prepared the study protocol. KP performed data collection and analysis. All authors contributed to its revision. KP drafted the manuscript and all authors read and approved the final manuscript.

COMPETING INTERESTS

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ETHICS APPROVAL

None required.

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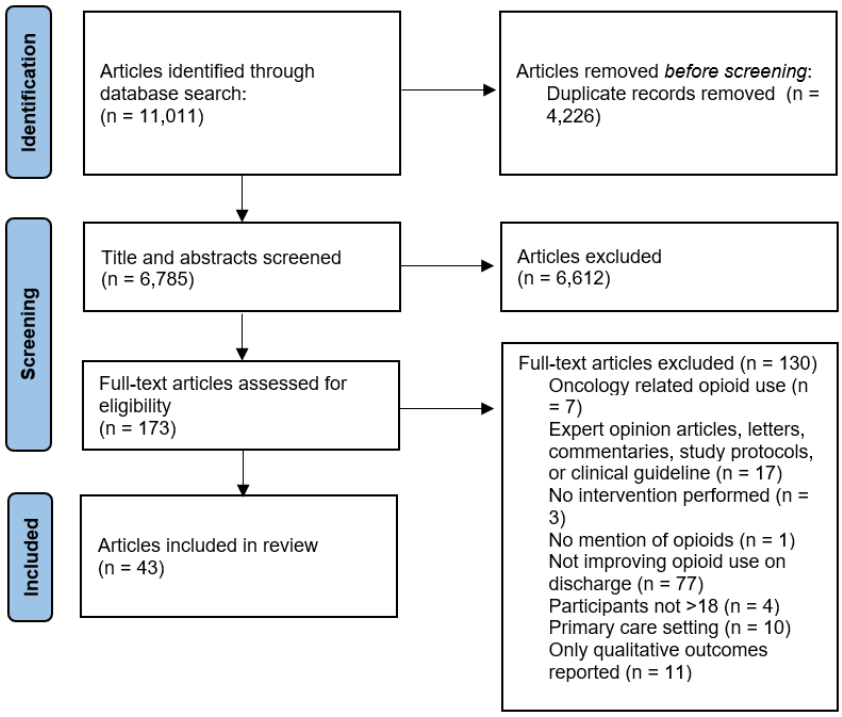


FIGURE 1 Study inclusion and exclusion criteria flow diagram

TABLE 1 Summary of multifaceted interventions aimed at prescribing upon hospital discharge (n=15)

Author, year, country	**Study design Study size (n; I, C)**	**Study population Study duration**	**Intervention**	**Intervention**	**Outcomes**	**Outcomes**
			Health care professional education	**Non-education based intervention**	**Prescribing**	**Clinical**

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Intervention	Intervention	Outcomes	Outcomes
Ringwalt et al.,[16] 2015, USA	Randomized controlled trial 406 (I=200, C=206)	ED 12 months	None	Alert placed in patients' electronic medical record when they had made multiple visits to various ED's and that they should receive treatment in the community. Letter sent to patients and community-based providers stating that their pain is best managed from a community-based provider.	| Proportion of ED visits resulting in an opioid prescription provided on discharge: 26% to 16%; p<0.0001	NR
Landau et al.,[18] 2021, USA	Retrospective cohort study 2,916 (I=2,224, C=702)	Cesarean delivery 7 months	Provider education about multimodal opioid-sparing analgesia, judicious opioid prescribing and new in-hospital order sets	Stepwise multimodal opioid-sparing analgesic computerised set	| Oxycodone-free discharge prescriptions from 4.4% to 8.5% with an absolute | of 4.1% (95% CI 2.5 to 5.6); p<0.01 | Median (IQR) number of oxycodone pills prescribed from 32 (24-40) to 18 (16-20); p<0.01	NR

Author, year, country	**Study design Study size (n; I, C)**	**Study population Study duration**	**Intervention**	**Intervention**	**Outcomes**	**Outcomes**
Pattullo et al.,[42] 2021, Australia	Prospective pre-post study 21,724 (I=10,765, C=10,959)	ED and surgical ward 12 weeks	Audit, evaluation and feedback Staff education	Implementation of an opioid prescribing toolkit using the Plan-Do-Study-Act (PDSA) model: Guideline development Patient education	No significant change in rate of opioid prescriptions per discharge; p=0.25 | Rates of tailored oxycodone prescribed on discharge: 62% to 90%; p<0.0001	NR
Prabhu et al.,[45] 2018, USA	Prospective pre-post study 624 (Phase 1: I=182, C=174 Phase 2: I=185, C=83)	Cesarean delivery Phase 1: 2 months Phase 2: 2 months	None	Phase 1: Healthcare provider-initiated counselling at discharge, including shared decision-making regarding the number of opioid tablets provided on discharge Phase 2: | of maximum prescription to 25 tablets of 5mg oxycodone or equivalent	| Mean (SD) number of opioid tablets prescribed on discharge Phase 1: 33.2 (9.3) to 26.5 (6.7); p<0.01 Phase 2: 24.9 (7.5) to 21.5 (6.3); p<0.01	NR

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Intervention	Intervention	Outcomes	Outcomes
Meisenberg et al.,[38] 2018, USA	Prospective pre-post study More than 44,000 encounters per month	All discharge patients from an acute care hospital, same-day surgery and ambulatory care clinic 16 months	Prescriber education and academic detailing by medical directors in one-on-one meetings	Tools to guide opioid prescribing based on inpatient use | of default standard opioid prescription orders Patient education Public education about opioid risks and alternatives through radio, television interviews, newspapers, websites, social media and signage	| Total health system MME per encounter by 58%: 34.4 MME to 14.5 MME; p<0.001	No | in number of patients with return visits to ED within 30 days for pain control after surgical procedure or previous ED visit; p=NR
Gugelmann et al.,[31] 2013, USA	Prospective pre-post study Primary hospital: 71,512 (I=30,958, C= 40,554) Affiliate hospital: 40,143 (I=27,143, C=13,000)	ED 8 to 11 months post intervention	Multifaceted interdisci-plinary educational modalities including lectures, journal clubs, case discussion	Electronic medical record decision support tool	Primary hospital: | Opioid discharge pack orders from 13.9% to 8.4% with an absolute | of 5.5% (95% CI, 4.6%-6.3%); p<0.0001 Affiliate hospital: | Opioid discharge pack orders from 4.8% to 2.1% with an absolute | of 2.7% (95% CI, 1.8%-3.6%); p<0.0001	NR

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Intervention	Intervention	Outcomes	Outcomes
Raman et al.,[46] 2021, UK	Retrospective pre-post study N=NR	ED Pre: 1 month Post-Phase 1: 4 months Post-Phase 2: 8 months	Phase 1: Multifaceted educational programme including one-to-one education, email summarising analgesic efficacy, addiction risk and guideline reinforcement. Followed by 4 separate group education sessions.	Phase 2: | in ED's opioid stock from 100 to 50 boxes of 30/500mg codeine and paracetamol	| Median number of 30/500mg codeine and paracetamol boxes supplied per month: 308 pre to 122 post-phase 1 to 131 post-phase 2 Overall | in 30/500mg codeine and paracetamol prescriptions of 59% post-phase 1 (p=0.018), and no statistically significant change post-phase 2; p>0.05	NR
Sigal et al.,[50] 2021, USA	Retrospective pre-post study 117,776 Baseline: 29,255 Phase 1: 28,278 Phase 2: 30,395 Phase 3: 29,848	ED Pre: 6 months Post-Phase 1: 6 months Post-Phase 2: 12 months Post-Phase 3: 18 months	Phase 2: Provider education on ADE's and risks of ED opioid use, nonopioid alternatives to analgesia	Phase 1: PDMP querying requirement Phase 3: Improvements to the electronic health system workflow including development of order sets that contained alternatives to opioid options and elimination of opioid options from "Quick Lists"	| Amount and proportion of opioid-eligible patients discharged with an opioid prescription Baseline: 5,665 (19.4%) Phase 1: 4,233 (15.0%) Phase 2: 3,448 (11.3%) Phase 3: 2,203 (7.4%); p<0.001	NR

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Intervention	Intervention	Outcomes	Outcomes
Schwab et al.,[49] 2020, USA	Retrospective pre-post study 150 (I=71, C=79)	Renal transplant 3 months	Education in post-operative analgesia	Multimodal pain control and removal of PCA post-operative order	No change in the OME's prescribed at discharge following PCA removal: 75 OME's in both; p=0.06	NR
Stanley et al.,[51] 2019, Australia	Retrospective pre-post study 461 (I=230, C=231)	Orthopaedic surgery 6-month audit periods	18 multidisciplinary education sessions provided to medical, nursing and pharmacy	Multidisciplinary expert advisory group providing oversight and raising awareness of issue Prescription opioid guidelines developed	| Mean number of opioid pills prescribed per patient: 30 to 18; p<0.001 | Inclusion of opioid discharge plan in discharge summary: 6.9% to 87.4%; p<0.001	NR
Lovecchio et al.,[37] 2019, USA	Retrospective pre-post study 2,479 (I=1,302, C=1,177)	Lumbar spine surgery 8 months	Mandatory 1-hour educational lecture on the scope and origin of the opioid epidemic, multimodal analgesia, role of prescribers and statewide substance registries	Development of prescribing guidelines	| Mean (SD) OME prescribed on discharge: 629 (294) to 490 (245); p<0.001	NR

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Intervention	Intervention	Outcomes	Outcomes
Burgess et al.,[25] 2019, USA	Retrospective pre-post study 303 (I= 94, C=209)	Cesarean delivery 5 months	Education of nurses and healthcare providers about initiative. Encouraged physicians not to write discharge opioid prescriptions immediately after cesarean, but to wait until closer to discharge	Comfort bundle designed incorporating a comprehensive pain relief strategy Removal of pre-set number for opioids	| Mean MME prescribed at discharge: 188.3 to 90; p=NR	NR
Boyle et al.,[24] 2019, USA	Retrospective interrupted time series Median number per month (I=107, IQR 53-151, C=119, IQR 49-155)	ED 6 months	Basic education about prescribing practices associated with opioid-related mortality provided to prescribers	Individual metrics showing prescribing data with comparison to group mean was distributed to clinicians Prescribing guidelines provided	| Median (IQR) rate of opioid prescriptions written per patient discharge by 28%: 12.5% (10-19%) to 9% (6-11%); p<0.001	NR
Tsega et al.,[55] 2020, USA	Retrospective pre-post study 9,804 (I=4,811, C=4,993)	All discharge patients from a tertiary care hospital 10 months	Awareness campaign and educational sessions for prescribers led by first-year medical students with weekly performance feedback	Providing prescribers with a pocket opioid reference card outlining opioid conversions and an overview of guidelines	No significant | in mean proportion (SD) of discharges prescribed opioids compared to baseline period: 12.2% (2.9%) compared to 11.4% (2.5%); p=0.165	NR

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Intervention	Intervention	Outcomes	Outcomes
Stevens et al.,[52] 2019, Australia	Retrospective pre-post study N=NR	Surgical 3x 6-week time intervals Intervention intervals defined as: Baseline period Introduction of interventions 1-5 Period following introduction of intervention 5 I1: September 2013 I2: March 2014 I3: June 2014 I4: July 2014 I5: August 2014	Five intervention cycles introduced: I5: Individual academic detailing session and feedback	I1: Education pamphlets given to patients I2: Analgesic discharge plan entered into the electronic discharge summary and given to patients I3: Letter detailing | in opioid prescriptions printed in JMO bulletin each term I4: Hospital pharmacists given guidelines	| Postintervention linear trend in oxycodone tablet prescribing on discharge by 3.2 tablets/100 surgical admissions; p=0.001 | Percentage of inappropriate oxycodone prescribing: 27% to 17%; p=0.048	NR
Tran et al.,[54] 2017, Australia	Retrospective pre-post study 661 (I=341, C=320)	Surgical 8-weeks	None	Pharmacist-assisted prescribing. The pharmacist discussed discharge medications with patients, prepared the prescription, printed the prescription, then discussed with the hospital doctor	| Median (IQR) amount of oxycodone supplied: 100mg (50-240) to 50mg (50-120); p<0.01	NR

I = intervention; C = control; USA = United States of America; CI = confidence interval; NR = not reported; ED = emergency department; UK = United Kingdom; MME = morphine milligram equivalent; ADE = adverse drug event; PDMP = prescription drug monitoring program; OME = oral morphine equivalents; IQR = interquartile range; SD = standard deviation; JMO = junior medical officer

TABLE 2 Summary of guidelines and protocols implemented to guide prescribing upon hospital discharge (n=13)

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Description of guideline or protocol for opioids	Intervention	Intervention	Outcomes	Outcomes
				Health care professional education	Non-education based intervention	Prescribing	Clinical
Jordan et al.,[21] 2020, USA	Retrospective case-control study 163 (I=82, C=81)	Sinus surgery 29 months	Patients were given paracetamol (500mg) PO every 6 hours for mild pain, naproxen (500mg) PO 2 or 3 times per day for moderate pain, and tramadol only for break-through pain	None	Perioperative pain management protocol using multimodal analgesia	| Mean hydrocodone milligram equivalents: 24.59 to 18.08; p<0.001	NR

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Description of guideline or protocol for opioids	Intervention	Intervention	Outcomes	Outcomes
Ganti et al.,[17] 2020, USA	Retrospective cohort study 45 (I=19, C=26)	Transoral robotic surgery 42 months	Patients were discharged with a 14-day supply of gabapentin, celecoxib and paracetamol. They were given a 7-day supply of hydrocodone-paracetamol if their pain was not adequately controlled postoperatively with non-opioid analgesia	None	Implementation of ERAS protocol	Proportion of patients receiving an opioid prescription upon discharge: 96.2% to 31.6%; p<0.001	Mean (SD) postoperative DVPRS pain scores between control group and ERAS group: 4.2 (1.6) vs 2.9 (2.1); p=0.042

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Description of guideline or protocol for opioids	Intervention	Intervention	Outcomes	Outcomes
Gridley et al.,[30] 2020, USA	Prospective pre-post study 80 (I=52, C=28)	Ureteroscopic surgery 5 months	Patients were provided with paracetamol and ibuprofen on discharge. No opioids were prescribed on discharge. If patients required further pain relief after discharge, they could call the urology clinic and were provided with tramadol or oxycodone	None	ERAS protocol focusing on multimodal analgesia	| Patients discharged with an opioid: 93% to 0%; $p<0.01$	No change in postoperative phone calls for uncontrolled pain

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Description of guideline or protocol for opioids	Intervention	Intervention	Outcomes	Outcomes
Pena et al.,[43] 2021, USA	Prospective pre-post study 191 (I=92, C=99)	Cardiac surgery or ICU 11 months	If the patient consumed no tablets in the 48 hr prior to discharge, they were not prescribed any opioids. If they received less than 7 tablets, they received between 0-20 tablets on discharge. If they consumed greater than 10 tablets, they were given 15-30 tablets on discharge	Lecture to prescribers on the guidelines	Opioid prescription amounts were based on the number of opioid tablets consumed in 48hr period prior to discharge	| Mean (SD) opioid tablets prescribed on discharge: 26 (10) to 18 (8); p<0.001	NR

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Description of guideline or protocol for opioids	Intervention	Intervention	Outcomes	Outcomes
Linder et al.,[36] 2019, USA	Prospective pre-post study 96 (I=39, C=57)	Women undergoing surgery for symptomatic pelvic organ prolapse 8 months	If patients had no opioid use during hospitalisation, they were not provided any opioids on discharge. For patients who used opioids in hospital, they were supplied enough opioids that would be required based on the procedure type. Vaginal prolapse surgery or abdominal sacrocolpopexy = 15 oxycodone 5-mg tablets Robotic sacrocolpopexy = 18 oxycodone 5 mg tablets If patients were using a greater than expected amount in hospital, prescribing was individualized based on the 24-hours prior to discharge	None	Procedure-specific opioid-prescribing recommendations. A tiered approach to opioid prescribing was created.	| Median (IQR) opioids prescribed in OME: 200 (150-225) to 112.5 (22.5-112.5); p<0.0001	No change in median (IQR) patient satisfaction with pain control after discharge using Likert scale: 9 (8-10) to 9 (8-10); p=0.87

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Description of guideline or protocol for opioids	Intervention	Intervention	Outcomes	Outcomes
Holland et al.,[32] 2019, USA	Prospective pre-post study 372 (I=181, C=191)	Cesarean delivery 3 months	Clinicians told not to prescribe opioids for patients who did not require any post-delivery. If they required some during stay, but not in 24 hours prior to discharge, they were given no more than 10 tablets of 5 mg oxycodone. If they required opioids at the time of discharge, they were given no more than 20 tablets of 5 mg oxycodone at discharge. Number of tablets given was determined in discussion with the patient	None	Discharge opioid prescribing determined according to patterns of opioid use in-hospital as well as shared decision-making with the patient	| Patients discharged with an opioid prescription: 91% to 40%; p<0.001	NR

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Description of guideline or protocol for opioids	Intervention	Intervention	Outcomes	Outcomes
Sada et al.,[47] 2021, USA	Retrospective pre-post study 754 (I=397, C=357)	Endocrine surgery 6 months	Standard dosing options suggested 37.5 MME for thyroid/parathyroid procedures with maximum amount of 75 MME, and 60 MME for minimally invasive adrenalectomy with maximum amount of 150 MME Patient factors considered include anticipated pain intensity, non-opioid analgesics utilized, and pain scores. High opioid dosing limited to preoperative opioid users	None	Implementation of opioid prescribing guidelines: Development of low, standard, and high opioid dosing options for each procedure	Number and proportion of patients discharged with opioid prescription: 343 (96.1%) to 307 (77.3%); p<0.01 | Median (IQR) MME prescribed: 150 (100-200) to 50 (25-75); p<0.01	NR

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Description of guideline or protocol for opioids	Intervention	Intervention	Outcomes	Outcomes
Peterman et al.,[44] 2020, USA	Retrospective pre-post study 180 (I=75, C=105)	Ventral hernia repair patients 6 months	If the patient used 0-5 MME in the 24 hours prior to discharge, they received 15 MME on discharge. If they used 6-15 MME, they were given 40 MME on discharge. If they used 15-30 MME, they were given 80 MME. If they used over 30 MME, they were given 100 MME on discharge	None	Evidence-based prescribing protocol implementation Determining the amount of opioids prescribed relative to opioid use in the day prior to discharge	| Total median (IQR) MME prescribed on discharge by 57%: 225 (150-400) to 100 (50-184) p<0.001	NR

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Description of guideline or protocol for opioids	Intervention	Intervention	Outcomes	Outcomes
Stewart et al.,[53] 2019, Australia	Retrospective pre-post study 198 (I=60, C=138)	Surgical 24 months	Tramadol 50 mg 4-hourly prn was provided on discharge: Twenty tablets were given if they were discharged sooner than 24 hours since PCA was ceased or if they needed 2 or more doses in the last 24 hours with PCA ceased. They were given 10 tablets if they needed 1-2 doses in the last 24 hours with PCA ceased. Oxycodone 5 mg 4-hourly prn was provided on discharge: 20 tablets were provided if they needed 5 or more doses in the last 24 hours with PCA ceased. They were given 10 tablets if they needed 2-4 doses in the last 24 hours with PCA ceased	None	Guidelines focused on multimodal analgesia Paracetamol and celecoxib were provided on discharge. Tramadol and oxycodone were prescribed only if they needed doses within the last 24 hours or if they had ceased PCA sooner than 24 hours	| Compliance rates to prescribing guidelines for oxycodone IR after 2 years: 88.9% to 74%; p=NR	NR

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Description of guideline or protocol for opioids	Intervention	Intervention	Outcomes	Outcomes
Pace et al.,[41] 2018, USA	Retrospective pre-post study 529 (I=263, C=266)	ED 4 months	Encouraged non-opioid analgesics Did not replace prescriptions for patients with pain contracts unless confirmed by primary care physician If opioids were needed, a short course of opioids (< 15 tablets hydrocodone) was prescribed	None	Introduction of an opioid prescribing pathway for patients with chronic pain	No significant difference in mean (SD) MEQ per script: 132.32 (95.56) to 105.82 (76.65); p=0.082 | Proportion of patients who received an opioid prescription for chronic pain: 36.55% to 23.45%; p=0.0017	NR
Osborn et al.,[40] 2017, USA	Retrospective pre-post study 99,011 (I=36,194, C=62,817)	ED 7 years	Prescribers were told to avoid prescribing long-acting opioids, and opioid prescriptions for acute injuries should not exceed 30 tablets	None	Implementation of general prescribing guidelines. Placards outlining guidelines posted in ED treatment rooms.	| Proportion of ED visits resulting in a discharge opioid prescription: 25.7% to 15.6%; p<0.001 | Mean (SD) number of tablets per prescription: 19.5 (8.6) to 16.6 (7.2); p<0.001	NR

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Description of guideline or protocol for opioids	Intervention	Intervention	Outcomes	Outcomes
Beaudoin et al.,[23] 2017, USA	Retrospective pre-post study 40,622 (I=21,845, C=18,777)	ED 2 years	Details of guidelines NR	None	ED opioid prescribing policy and guidelines intended to reduce inappropriate opioid prescribing	| Proportion of patients receiving an opioid on discharge: 35% to 29.3%, difference of -5.7% (95% CI -6.7, -4.7); p=NR	NR
Del Portal et al.,[27] 2015, USA	Retrospective pre-post study 13,187 Pre: 4540 Post-Phase 1: 4122 Post-Phase 2: 4525	ED Pre: 6 months Post-Phase 1: 6 months Post-Phase 2: 6 months	Discharge prescriptions should contain less than 7 days' worth of opioids. Avoid prescribing long-acting opioids	None	Implementation of general prescribing guidelines. Hard copies and electronic copies were available in the ED.	| Proportion of patients prescribed opioids on discharge from Pre to Post-Phase 1 (0-6 months after intervention): 52.7% to 29.8%; p<0.001 | Proportion of patients prescribed opioids on discharge from Pre to Post-Phase 2 (12-18 months after guideline): 52.7% to 33.8%; p<0.001	NR

I = intervention; C = control; USA = United States of America; ERAS = enhanced recovery after surgery; DVPRS = defense & veterans pain rating scale scores; MME = morphine milligram equivalent; ICU = intensive care unit; SD = standard deviation; ED = emergency department; IQR = interquartile range; PCA = patient-controlled analgesia; OME = oral morphine equivalents; MEQ = morphine equivalent milligrams; PO = by mouth, orally

TABLE 3 Summary of changes to default settings in electronic medical records for hospital discharge prescribing (n=3)

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Intervention	Outcomes
Santistevan et al.,[48] 2018, USA	Retrospective pre-post study 6,568 (I=2,464 , C=4,104)	ED 10 months	Removal of default opioid quantity from electronic order-entry prescription forms	| Median (IQR) quantity of opioid tablets prescribed post-intervention: 20 (10-20) to 15 (10-20); p<0.0001
Villwock et al.,[56] 2020, USA	Retrospective pre-post study 53,608 (I=28,198, C=25,410	Inpatient and ED discharges Post phase 1: 3 months Post phase 2: 48 months	Autopopulation removal for opioid prescribing	Post phase 1: No significant change in mean MME prescribed post-APR for inpatient discharge: 406 (95% CI 386-426) to 436 (95% CI 401-470); p=0.116 or ED discharge: 114 (95% CI 107-120) to 108 (95% CI 103-114); p=0.752 Post phase 2: No significant trend across months for inpatients: 0.997, p=0.065 and 1.003, p=0.142 pre and post. ED model had a downward trend in MME prescribed prior to and after APR 0.997, p=0.065 and 1.003, p=0.142 pre and post

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Intervention	Outcomes
Montoy et al.,[39] 2020, USA	Retrospective pre-post study N=NR	ED 20 weeks	Alteration of the prepopulated dispense quantities for discharge prescriptions of commonly prescribed opioids. Default quantities were set to null, 5, 10, 15 and 20 tablets	| Quantity of tablets prescribed when the default quantity was set to: 5 compared to 10: difference of 1.8 (95% CI 0.8-2.7); p<0.001 5 compared to 15: difference of 1.8 (95% CI 0.8-2.9); p<0.001 5 compared to 20: difference of 2.9 (95% CI 2.1-3.8); p<0.001 All default quantities including the null treatment, yielded lower quantities prescribed than the default 20 setting

I = intervention; C = control; USA = United States of America; ED = emergency department; IQR = interquartile range; MME = morphine milligram equivalent; APR = autopopulation removal; CI = confidence interval; NR = not reported

TABLE 4 Summary of educational interventions aimed at prescribing on hospital discharge (n=7)

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Intervention	Outcomes
Michael et al.,[15] 2018, USA	Randomised controlled trial Number of prescribers included: 109 (C=58, I=51) The mean number of patients discharged for all prescribers was 1,124 (SD 681)	ED Phase 1: 6 months pre-intervention Phase 2: 6 months post-intervention Phase 3: 12 months post-intervention	Prescribers self-reflected on their opioid prescribing compared to peers Actual opioid prescribing data compared to peers provided. No further intervention conducted	| Median (IQR) percentage of patients discharged with an opioid prescription: Phase 1: 10.5 (6.9) Phase 2: 6.4 (4.4) Phase 3: 5.6 (4.8); p<0.001 | Median (IQR) opioid prescriptions per hundred total prescriptions written: Phase 1: 21.0 (8.5) Phase 2: 4.6 (8.9) Phase 3: 11.7 (8.0); p<0.001

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Intervention	Outcomes
Hopkins et al.,[14] 2020, Australia	Cluster randomised controlled trial Pre: 2383 (I=1369, C=1014) Post: 1679 (I=973, C=706)	Surgical 6 months	Surgical interns, residents, clinical pharmacists received 30-minute face-to-face education sessions by the analgesic stewardship pharmacist.	|Median (IQR) total opioid quantity prescribed on discharge for the intervention group: 5 (0-12) to 4 (0-10); p=0.001 No change in median (IQR) total opioid quantity prescribed on discharge for the control group
Yorkgitis et al.,[20] 2019, USA	Prospective cohort study 23 prescribers interviewed before and after educational intervention	Surgical Duration NR	One-hour, in-person opioid prescribing education session using a "Getting it RIGHTT" strategy (Risk for adverse event, Insight into pain, Going over pain plan, Halting Opioids, Tossing unused opioids, Trouble Identification)	No statistically significant change in mean (SD) number of opioid pills prescribed for surgery types including laparoscopic cholecystectomy (18.3 (7.6) to 15.7 (7.0); p=0.23) and laparoscopic ventral hernia (19.8 (6.7) to 17.2 (7.7); p=0.23)
Oyler et al.,[19] 2018, USA	Retrospective cohort study 913 (I=424, C=489)	Trauma patients 12 months	Medical staff education about pain management strategy aimed at | opioid use consisting of: Pharmacist-led discussion, a 1-hour lecture provided to surgical residents bimonthly for study period, and written material available in a reference manual Patient education provided on admission and discharge	| Median (IQR) daily discharge MME: 90 (60-120) to 45 (30-90); p<0.001

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Intervention	Outcomes
Kline et al.,[34] 2019, Australia	Interrupted time series 43,814 Phase 1: 17, 371 Phase 2: 5,938 Phase 3: 20, 505	ED Phase 1: 18 weeks pre-intervention Phase 2: 6 weeks peri-intervention Phase 3: 22 weeks post-intervention	Nurses, pharmacists and prescribing doctors were educated using education sessions, staff information emails, posters within ED and a patient brochure	| Patients prescribed oxycodone on discharge: 3.8% to 2.9%; p<0.05 | Mean (SD) total number of tablets of oxycodone per prescription: Phase 1: 16.7 (16.5) Phase 2: 12.7 (6.0) Phase 3: 10.7 (5.2); p<0.05
Donaldson et al.,[29] 2017, Australia	Prospective pre-post study 161 (I=81, C=80)	ED 5 months	A 5-minute one-on-one educational intervention regarding opioid related harm in the community, role of prescribers, and optimal prescribing practices was delivered to ED opioid analgesic prescribers	| Median total amount of oxycodone prescribed per patient: 100 to 50 p=0.04 | Proportion of patients receiving written opioid analgesic information: 10% to 22%; p=0.04
Kamm et al.,[33] 2020, USA	Retrospective pre-post study N=NR	Surgical 3 weeks	Prescriber education and training using MEDD and MEDD calculator in EMR	| MEDD on discharge per month by an average of 1.7 per month; p=0.23
Dieujuste et al.,[28] 2020, USA	Retrospective pre-post study N=NR	ED 21 months	Sharing opioid prescribing dashboard with ED medical director and academic detailer Education of ED providers and implementation of toolkit resources Audit and feedback sessions with highest prescribing providers Quarterly reporting of opioid prescribing dashboard data to ED providers	| Median (IQR) prescribing rate of opioids from 5.5 (34.76) to 3.68 (31.23); p<0.01 | Opioid prescribing rate on average 0.87 times per quarter (95% CI = 0.84 to 0.89); p<0.01

Author, year, country	Study design Study size (n; I, C)	Study population Study duration	Intervention	Outcomes
Andereck et al.,[22] 2019, USA	Retrospective pre-post study 54,466 (I=18,830, C=35,636)	ED 11 months	Opioid prescribing feedback provided to prescribers in comparison to their peers. Formal lecture provided on evidence-based nonopioid treatments in a weekly educational conference followed by small-group discussions.	| Aggregate opioid prescribing rates: 8.6% (95% CI: 8.3% - 8.9%) to 5.8% (95% CI: 5.5% - 6.1%); p=NR
Lancaster et al.,[35] 2019, USA	Retrospective pre-post study 1,429 (I=724, C=705)	Surgical 6 months	Multiple educational interventions focused on multimodal analgesia and appropriate opioid prescribing. Included department wide grand rounds, didactic, and case-based conferences and creation of pocket cards	| Quantity of opioids prescribed for general surgery operations by 131 OME; p<0.001
Burton et al.,[26] 2016, USA	Retrospective pre-post study 149,884 (Baseline: 82,241, Phase 1: 35,525, Phase 2: 32,118)	ED 15 months	Phase 1: Prescriber feedback through providing each ED physician with their prescribing data compared to the group mean. Phase 2: Prescriber feedback through providing each ED physician with their prescribing data and the unblinded data results for each physician in the group.	| Mean opioid tablets provided on discharge between Baseline, Phase 1 and Phase 2: 16 to 14 to 13; p<0.01 | Mean opioid prescribing rate between Baseline, Phase 1 and Phase 2: 20% to 13% to 8%; p<0.01

I = intervention; C = control; USA = United States of America; ED = emergency department; IQR =

interquartile range; CI = confidence interval; NSAID = non-steroidal anti-inflammatory drug; MME = morphine milligram equivalent; MEDD = morphine equivalent daily dosing; EMR = electronic medical record; OME = oral morphine equivalents

APPENDIX 1 Database search terms

MEDLINE (1960 to Present) (OvidSP)

1. exp Analgesics, Opioid/ or exp Narcotics/
2. (acetyldihydrocodeine or alfentanil or allylprodine or alphamethylfentanyl or alphaprodine or benzylmorphine or betaprodine or buprenorphine or butorphanol or bremazocine or codeine or contin or dextromoramide or dextropropoxyphene or dezocine or diacetylmorphine or diamorphine or dihydrocodeine or dihydromorphine or dihydromorphone or diphenoxylate or dipipanone or enadoline or ethylketazocine or ethylmorphine or etonitazene or etorphine or fentanyl or heroin or hydrocodone or hydromorphin* or hydromorphone or ketazocine or ketobemidone or lefetamine or levomethadon or levomethadyl or levomethorphan* or levorphanol or loperamide or meperidine or meptazinol or methadone or methadyl or methylmorphine or morphin* or nalbuphine or narcotic* or nicocodeine or nicomorphine or normorphine or noscapin* or ohmefentanyl or opiate* or opioid* or opium or oripavine or oxycodone or oxycontin or oxymorphone or papaveretum or papaverin or pentazocine or percocet or peronine or pethidine or phenazocine or phencyclidine or pholcodine or piritramid* or prodine or promedol or propoxyphene or remifentanil or sufentanil or tapentadol or thebaine or tilidine).tw.
3. **1 or 2**
4. Patient Discharge/ or (hospital* adj2 discharg*).mp or (discharge adj2 prescrib*).mp
5. hospital.mp. or Hospitals/ or (hospital* adj2 setting*).mp.
6. exp Hospital Departments/
7. exp Ambulatory Surgical Procedures/
8. (acute adj2 care).mp. or acute disease/
9. emergency service, hospital/ or trauma centers/ or (emergency adj2 department*).mp.
10. **4 or 5 or 6 or 7 or 8 or 9**
11. ((prescrib* adj2 interven*) or (approp* adj2 prescrib*)).mp.
12. medication errors/ or inappropriate prescribing/ or pharmacy service, hospital/
13. Medication Therapy Management/
14. "Drug Utilization Review"/ or drug utili?ation review*.mp. or Drug Utilization/ or stewardship.mp.
15. drug monitor*.mp. or Drug Monitoring/
16. Medication Systems, Hospital/
17. intervention*.ti. or (intervention* adj6 (clinician* or collaborat* or design* or doctor* or educa* or impact* or improve* or individuali* or interdisciplin* or multicomponent or multi-component or multidisciplin* or multi-disciplin* or multifacet* or multi-facet* or multimodal* or multi-modal* or pharma* or physician* or practitioner* or prescrib* or professional* or provider* or tailor* or target* or usual care)).ti,ab.
18. (adherence or alert* or benchmark* or (change adj3 treatment) or computer assist* or support or compute* or clinical decision* or dosing or formulary or guidance or guideline* or impact* or justification or overuse or over-prescrib* or overprescrib* or under-prescrib* or underprescrib* or pathway* or program* or programme* or (quality adj3 improv*) or reminder* or restriction* or unnecessary).ti.
19. **11 or 12 or 13 or 14 or 15 or 16 or 17 or 18**
20. 3 and 10 and 19
21. limit 20 to (english language and humans)

APPENDIX 2 Quality assessment summary of included randomised controlled trials using the *Revised Cochrane Risk of Bias Tool for Randomized Trials*[11] (n=3)

Study Authors	**Hopkins et al.**	**Hopkins et al.**
Bias	**Judgement**	**Support for judgement**

Study Authors	**Hopkins et al.**	**Hopkins et al.**
Bias arising from the randomisation process	Some concerns	There were many baseline differences betwe
Bias due to deviations from intended interventions	Some concerns	"Major institutional changes caused a four-
Bias due to missing outcome data	Low risk	No missing data reported.
Bias in measurement of the outcome	Low risk	Discharge opioid prescribing data was colle
Bias in selection of the reported result	Low risk	All relevant results and statistical analyses
Overall risk of bias	**Some concerns**	**Some concerns**
Study Authors	**Michael et al.**	**Michael et al.**
Bias	**Judgement**	**Support for judgement**
Bias arising from the randomisation process	Low risk	Randomisation was conducted by stratifyin
Bias due to deviations from intended interventions	Low risk	There were no deviations from the intended
Bias due to missing outcome data	Low risk	"Table 2 reports cross-sectional aggregate p
Bias in measurement of the outcome	Low risk	"... we passively observed prescribing patte
Bias in selection of the reported result	Low risk	All relevant reports and statistical analysis
Overall risk of bias	**Low risk**	**Low risk**
Study Authors	**Ringwalt et al.**	**Ringwalt et al.**
Bias	**Judgement**	**Support for judgement**
Bias arising from the randomisation process	Low risk	A web-based random number generator wa
Bias due to deviations from intended interventions	Low risk	No deviations reported
Bias due to missing outcome data	Low risk	No missing data reported
Bias in measurement of the outcome	Low risk	Collection of data was the same for both in
Bias in selection of the reported result	Low risk	All relevant reports and statistical analysis
Overall risk of bias	**Low risk**	**Low risk**

APPENDIX 3 Quality assessment summary of included nonrandomised controlled studies using the *Risk of Bias in Non-randomised Studies of Interventions* tool[12] (n=40)

Study authors	**Andereck et al.**	**Andereck et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	No adjustments made to account for potential confounding factors.
Bias in selection of participants into the study	Low risk of bias	All eligible participants were enrolled in the study
Bias in classification of interventions	Low risk of bias	Clear classification of intervention groups
Bias due to deviations from intended interventions	No information	Potential deviations from intended interventions not described.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Low risk of bias	Quantitative analysis of prescribing rates
Bias in selection of the reported result	No information	Not described.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Beaudoin et al.**	**Beaudoin et al.**
Bias	**Judgement**	**Support for judgement**

Study authors	**Andereck et al.**	**Andereck et al.**
Bias due to confounding	Serious risk of bias	Prescribers were stratified into prescriber level, but no additional adjustments were made for potential confounding factors.
Bias in selection of participants into the study	Low risk of bias	All eligible patients were included.
Bias in classification of interventions	Low risk of bias	Hospitals were classified as either intervention or control hospitals
Bias due to deviations from intended interventions	No information	Not described.
Bias due to missing data	Low risk of bias	No missing data reported
Bias in measurement of outcomes	Low risk of bias	"... interrupted time-series analysis utilizing data obtained from the electronic health records..."
Bias in selection of the reported result	No information	Not described.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Boyle et al.**	**Boyle et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Low risk of bias	Stratified by prescriber type.
Bias in selection of participants into the study	Low risk of bias	All physicians and advanced practice clinicians were included in the intervention.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention groups.
Bias due to deviations from intended interventions	No information	Potential deviations from intended interventions not described.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Low risk of bias	Quantitative analysis of prescribing rates using interrupted time series.
Bias in selection of the reported result	No information	Not described.
Overall quality assessment	**Low risk of bias**	**Low risk of bias**
Study authors	**Burgess et al.**	**Burgess et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	"...asked the residency director to encourage resident physicians not to write discharge prescriptions for opiates immediately after the caesarean." No follow-up of how many residents were advised of this.
Bias in selection of participants into the study	Low risk of bias	All women who underwent a caesarean section were included.

Study authors	**Andereck et al.**	**Andereck et al.**
Bias in classification of interventions	Low risk of bias	Clear classification of intervention groups.
Bias due to deviations from intended interventions	Low risk of bias	Adherence to intervention was assessed monthly by the maternity nurse educator through a medical record review.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Serious risk of bias	Nurses documented use of nonpharmacologic comfort measures, which may have influenced patient-reporting factors.
Bias in selection of the reported result	Critical risk of bias	No statistical analysis reported
Overall quality assessment	**Critical risk of bias**	**Critical risk of bias**
Study authors	**Burton et al.**	**Burton et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	No adjustments were made for potential confounding factors
Bias in selection of participants into the study	Low risk of bias	"We included for analysis all opioid prescriptions written at ED discharge over the 15-month data collection period. . . "
Bias in classification of interventions	Low risk of bias	Time periods for interventions clearly addressed
Bias due to deviations from intended interventions	No information	Not reported
Bias due to missing data	Low risk of bias	"We included for analysis all 47 physicians who remained in the group during the measured interval."
Bias in measurement of outcomes	Low risk of bias	"We abstracted clinical data for all ED discharged from the EHR via a computer algorithm"
Bias in selection of the reported result	No information	Not reported
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Del Portal et al.**	**Del Portal et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Low risk of bias	Multinomial logistic regression used to assess effect of the guideline
Bias in selection of participants into the study	Low risk of bias	All eligible participants included in the study
Bias in classification of interventions	Low risk of bias	Time periods of the intervention clearly identified
Bias due to deviations from intended interventions	No information	Not reported
Bias due to missing data	Low risk of bias	No missing data reported

Study authors	**Andereck et al.**	**Andereck et al.**
Bias in measurement of outcomes	Moderate risk of bias	"Retrospective chart review was performed by querying the electronic medical record for all visits..."
Bias in selection of the reported result	Serious risk of bias	Results of the multinomial logistic regression not reported
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Dieujuste et al.**	**Dieujuste et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	No adjustments made to account for potential confounding factors.
Bias in selection of participants into the study	Serious risk of bias	"...sites included in the program implementation group voluntarily self-selected for the program based on the decision of their facility's ED medical director."
Bias in classification of interventions	Low risk of bias	Clear classification of intervention groups.
Bias due to deviations from intended interventions	No information	Not described.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Low risk of bias	Descriptive analysis of prescribing rates.
Bias in selection of the reported result	Serious risk of bias	The primary investigator was an ED provider in one of the study sites.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Donaldson et al.**	**Donaldson et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	No adjustment for potential confounding factors
Bias in selection of participants into the study	Low risk of bias	"A group of 30 prescribers was randomly selected to receive the intervention, and their prescribing practices were studied."
Bias in classification of interventions	Low risk of bias	Intervention groups clearly identified
Bias due to deviations from intended interventions	No information	Not reported
Bias due to missing data	Low risk of bias	No missing data reported
Bias in measurement of outcomes	Moderate risk of bias	Interviews after discharge for secondary outcomes may have introduced recall bias
Bias in selection of the reported result	Low risk of bias	All relevant results reported
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Ganti et al.**	**Ganti et al.**

Study authors	**Andereck et al.**	**Andereck et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	"The study was not powered to detect differences in secondary outcomes between the groups."
Bias in selection of participants into the study	Low risk of bias	Consecutive selection of participants into the study.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention groups.
Bias due to deviations from intended interventions	Low risk of bias	Compliance rates with ERAS protocol are stated in table 3. All compliance rates are above 84.2%.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Serious risk of bias	"Prescribing physicians and patients were aware of the analgesic regimen that each patient was allocated to. This may have introduced an element of implicit bias whereby physicians were less likely to prescribe narcotic medications in the postoperative period and on discharge to patients assigned to the ERAS protocol."
Bias in selection of the reported result	Low risk of bias	Primary and secondary outcomes listed in article table.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Gridley et al.**	**Gridley et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Low risk of bias	Potential risk of bias due to confounding accounted for by statistical analysis such as linear and logistic multivariable regression models.
Bias in selection of participants into the study	Low risk of bias	All eligible patients were included in the study.
Bias in classification of interventions	Low risk of bias	Clear classification of those in the intervention group.
Bias due to deviations from intended interventions	No information	Not described.
Bias due to missing data	Low risk of bias	Outcome data available for all participants.
Bias in measurement of outcomes	Low risk of bias	"Opioid prescription data were obtained from the Vanderbilt electronic medical record and Tennessee Controlled Substance Monitoring Database."

Study authors	**Andereck et al.**	**Andereck et al.**
Bias in selection of the reported result	Moderate risk of bias	"Although the study was powered to detect the primary outcome, we assessed numerous postoperative outcomes and may not have had the power to detect a difference in every outcome."
Overall quality assessment	**Moderate risk of bias**	**Moderate risk of bias**
Study authors	**Gugelmann et al.**	**Gugelmann et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	"Not all providers were present for every component of the intervention; that is, the effects of the intervention as a whole could have been diluted by incomplete information dissemination among clinicians."
Bias in selection of participants into the study	Low risk of bias	All eligible patients were included in the intervention.
Bias in classification of interventions	Low risk of bias	Clear classification of those in the intervention group.
Bias due to deviations from intended interventions	No information	Not described.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Serious risk of bias	"Providers were aware of our initiative and may have felt pressured to decrease their opioid discharge pack orders."
Bias in selection of the reported result	Moderate risk of bias	"We did not assess whether there was a change in opioids administered during the ED visit or the number or quantity of opioid prescriptions at the time of discharge."
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Holland et al.**	**Holland et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Low risk of bias	Potential confounding factors were identified and controlled for.
Bias in selection of participants into the study	Low risk of bias	All eligible patients were included in the results.
Bias in classification of interventions	Low risk of bias	Clear classification of those in the intervention group.
Bias due to deviations from intended interventions	No information	Not discussed.
Bias due to missing data	Low risk of bias	No missing data reported.

Study authors	**Andereck et al.**	**Andereck et al.**
Bias in measurement of outcomes	Moderate risk of bias	Satisfaction with pain control was assessed by patient recall, introducing recall bias. All other information was manually collected from electronic medical records.
Bias in selection of the reported result	No information	Not discussed.
Overall quality assessment	**Moderate risk of bias**	**Moderate risk of bias**
Study authors	**Jordan et al.**	**Jordan et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	"There was also a significantly lower number of patients who underwent septoplasty and inferior turbinate reduction in the post-protocol group, which could have led to improved pain control as those procedures have been associated with increased pain in several studies."
Bias in selection of participants into the study	Moderate risk of bias	"It was a retrospective single-institution study comparing similar cohorts of patients but without a control during the same period, potentially introducing time bias."
Bias in classification of interventions	Low risk of bias	Clear classification of those in the intervention group.
Bias due to deviations from intended interventions	No information	Not discussed.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Moderate risk of bias	"Patient satisfaction was determined by postoperative phone calls regarding pain, which may have led to underreporting of pain…"
Bias in selection of the reported result	No information	Not discussed.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Kamm et al.**	**Kamm et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	Potential confounding factors identified but was not controlled for.
Bias in selection of participants into the study	Low risk of bias	All eligible prescribers included in analysis.
Bias in classification of interventions	Low risk of bias	Clear classification of those in the intervention group.

Study authors	**Andereck et al.**	**Andereck et al.**
Bias due to deviations from intended interventions	No information	Not discussed.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Serious risk of bias	There was an "inability to track how many times the MEDD tool was viewed in the EMR or by whom and therefore it is unclear whether the improvements were influenced specifically by use of the tool."
Bias in selection of the reported result	No information	Not discussed.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Kline et al.**	**Kline et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	"From late 2016 the pharmacy service to ED was extended to a seven-day model to improve all aspects of medication management. This may have affected the baseline data and could have confounded the effects of the intervention."
Bias in selection of participants into the study	Low risk of bias	All relevant health care professionals were included in the intervention.
Bias in classification of interventions	Low risk of bias	Clear classification of those in the intervention group.
Bias due to deviations from intended interventions	No information	Not discussed.
Bias due to missing data	Moderate risk of bias	"The best efforts of the investigators to analyse the medical records were used in these cases to determine the source of the oxycodone prescription. The few that were indeterminate were excluded from the study."
Bias in measurement of outcomes	Low risk of bias	"For all eligible prescriptions, a standardised data collection form was completed using data from the ED record and their iEMR notes... This data was entered into the secure database REDCap by a research assistant who had no involvement in the design or execution of the intervention."
Bias in selection of the reported result	Low risk of bias	All relevant results reported.

Study authors	**Andereck et al.**	**Andereck et al.**
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Lancaster et al.**	**Lancaster et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	Potential confounding factors identified but not controlled for.
Bias in selection of participants into the study	Low risk of bias	All relevant patients were included in the analysis.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention group.
Bias due to deviations from intended interventions	No information	Not discussed.
Bias due to missing data	Serious risk of bias	"We had low response rates at 51% and 29%, which likely led to sampling bias. Additionally, our resident surveys were anonymous and therefore we could not match the surveys nor confirm that the same providers took the survey before and after the educational intervention."
Bias in measurement of outcomes	Moderate risk of bias	Attitudes of prescribers assessed through an anonymous survey. Actual prescribing data was extracted from electronic health records.
Bias in selection of the reported result	Low risk of bias	All relevant results reported.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Landau et al.**	**Landau et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Low risk of bias	Potential confounding factors identified and addressed.
Bias in selection of participants into the study	Low risk of bias	All eligible patients were included.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention groups.
Bias due to deviations from intended interventions	Moderate risk of bias	"The adherence to the new order set was in the order of 70% in both intervention hospitals despite robust provider education."
Bias due to missing data	Serious risk of bias	No information on control discharge opioid prescriptions provided.

Study authors	**Andereck et al.**	**Andereck et al.**
Bias in measurement of outcomes	Serious risk of bias	"The information on discharge prescription was abstracted from the institutional opioid prescription dashboard. This information was available in intervention hospitals 1 and 2 but not in control hospitals 3 and 4."
Bias in selection of the reported result	Low risk of bias	Primary and secondary outcomes reported in article tables.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Linder et al.**	**Linder et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Moderate risk of bias	Confounding variables addressed to an extent by the study design (e.g. restriction of included patients).
Bias in selection of participants into the study	Low risk of bias	All eligible patients were included in the study.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention groups.
Bias due to deviations from intended interventions	Low risk of bias	Prescribing recommendations were implemented and there was a 100% response rate for study participants survey responses.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Moderate risk of bias	Data was recorded prospectively, and patient satisfaction was assessed by follow up phone calls with a standardized script.
Bias in selection of the reported result	Low risk of bias	Outcomes listed in article tables.
Overall quality assessment	**Moderate risk of bias**	**Moderate risk of bias**
Study authors	**Lovecchio et al.**	**Lovecchio et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Low risk of bias	Possible confounding factors identified and adjusted for by study type (e.g. results reported by surgery type).
Bias in selection of participants into the study	Low risk of bias	"All employees eligible to prescribe opioid medications were required to attend a mandatory educational program in November 2016."
Bias in classification of interventions	Low risk of bias	Clear classification of intervention groups.

Study authors	**Andereck et al.**	**Andereck et al.**
Bias due to deviations from intended interventions	No information	Not discussed.
Bias due to missing data	Serious risk of bias	"While the vast majority of prescriptions given after surgery are written from the hospital, we could not capture prescriptions written by the minority of surgeon's private offices that use EMRs not linked to the hospital EMR."
Bias in measurement of outcomes	Low risk of bias	"All opioid medications prescribed at discharge were extracted from the hospital-wide electronic medical record."
Bias in selection of the reported result	Low risk of bias	All relevant results reported.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Meisenberg et al.**	**Meisenberg et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	Possible confounding factors identified but not addressed.
Bias in selection of participants into the study	Low risk of bias	"All members of the medical staff were included in the education efforts and had access to all tools introduced."
Bias in classification of interventions	Low risk of bias	Clear classification of intervention periods.
Bias due to deviations from intended interventions	No information	Not discussed.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Low risk of bias	Data was extracted from the electronic medical records.
Bias in selection of the reported result	Low risk of bias	All relevant results were reported.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Montoy et al.**	**Montoy et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Low risk of bias	Potential confounding factors addressed through linear regression models.
Bias in selection of participants into the study	Low risk of bias	All eligible prescribers were included.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention periods.

Study authors	**Andereck et al.**	**Andereck et al.**
Bias due to deviations from intended interventions	Moderate risk of bias	"We had an unexpected change of default settings from those of our protocol, but we were able to exclude those dates and resume the study as originally planned, albeit with an unplanned gap."
Bias due to missing data	Low risk of bias	Analysis addressed missing data and removed any risk of bias.
Bias in measurement of outcomes	Low risk of bias	Examined electronic medical record quantities.
Bias in selection of the reported result	Low risk of bias	All relevant results were reported.
Overall quality assessment	**Moderate risk of bias**	**Moderate risk of bias**
Study authors	**Osborn et al.**	**Osborn et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	Potential confounders identified but not adjusted for
Bias in selection of participants into the study	Low risk of bias	All eligible participants were included in the study
Bias in classification of interventions	Low risk of bias	Time period of intervention clearly identified
Bias due to deviations from intended interventions	No information	Not reported
Bias due to missing data	Low risk of bias	No missing data reported
Bias in measurement of outcomes	Moderate risk of bias	"The study was based on clinical and pharmacy data for ED visits retrieved retrospectively from the electronic medical record."
Bias in selection of the reported result	Low risk of bias	All relevant results reported in data tables
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Oyler et al.**	**Oyler et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	"It is possible that national and local initiatives to curb opioid prescribing could have exaggerated the effect of the interventions in our study."
Bias in selection of participants into the study	Low risk of bias	All eligible patients were included.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention groups.
Bias due to deviations from intended interventions	Serious risk of bias	"Nonopioid analgesics were not prescribed in a standardized fashion in the postintervention cohort."

Study authors	**Andereck et al.**	**Andereck et al.**
Bias due to missing data	Moderate risk of bias	"Only electronic discharge prescriptions were captured; however, there is nothing to suggest that hand-written prescriptions might have been more common in either cohort."
Bias in measurement of outcomes	Low risk of bias	Data manually extracted from electronic medical record.
Bias in selection of the reported result	Low risk of bias	Primary and secondary outcomes reported in article tables.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Pace et al.**	**Pace et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	"We were unable to control for potential confounding factors such as the concurrent Orthopaedic Surgery initiative to decrease ED follow-up time, differences in provider schedules, and pre-existing provider beliefs on chronic pain."
Bias in selection of participants into the study	Low risk of bias	All eligible patients were included in the chart review.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention periods.
Bias due to deviations from intended interventions	No information	Not discussed.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Moderate risk of bias	Outcome assessors not blinded to the study hypotheses.
Bias in selection of the reported result	Low risk of bias	All relevant results reported.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Pattullo et al.**	**Pattullo et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Low risk of bias	Potential confounding factors identified and addressed.
Bias in selection of participants into the study	Low risk of bias	All eligible patients were included in the study.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention periods.
Bias due to deviations from intended interventions	Low risk of bias	Sustainability of the intervention was measured, and it was found that changes from the initial intervention were sustained after 2 years.
Bias due to missing data	Low risk of bias	No missing data reported.

Study authors	**Andereck et al.**	**Andereck et al.**
Bias in measurement of outcomes	Low risk of bias	Manual collection of both handwritten scripts and records in the discharge software system.
Bias in selection of the reported result	Low risk of bias	All relevant results reported.
Overall quality assessment	**Low risk of bias**	**Low risk of bias**
Study authors	**Pena et al.**	**Pena et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Low risk of bias	Potential confounding factors identified and addressed through logistic regression models.
Bias in selection of participants into the study	Low risk of bias	All eligible patients were included in the study.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention groups.
Bias due to deviations from intended interventions	Serious risk of bias	"The authors did not audit prescribers to see whether they were using the Analgesia Prescription Guideline, nor did they evaluate their satisfaction with the tool."
Bias due to missing data	Moderate risk of bias	"Approximately one-third of participants were lost to follow-up, and it is possible that these participants had different opioid use and pain recovery trajectories."
Bias in measurement of outcomes	Moderate risk of bias	Structured phone call interviews were conducted where the patients were asked about their discharge opioid use. Their answers were compared to discharge prescriptions on their medical records.
Bias in selection of the reported result	Low risk of bias	Relevant results included in study tables.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Peterman et al.**	**Peterman et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Low risk of bias	Potential confounding factors addressed through linear regression models.
Bias in selection of participants into the study	Low risk of bias	All eligible patients were included.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention groups.
Bias due to deviations from intended interventions	No information	Not discussed.

Study authors	**Andereck et al.**	**Andereck et al.**
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Low risk of bias	Retrospectively reviewed opioid prescriptions using electronic medical records.
Bias in selection of the reported result	Low risk of bias	All relevant results reported.
Overall quality assessment	**Low risk of bias**	**Low risk of bias**
Study authors	**Prabhu et al.**	**Prabhu et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Low risk of bias	Potential confounding factors identified and addressed.
Bias in selection of participants into the study	Low risk of bias	All eligible patients included.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention periods.
Bias due to deviations from intended interventions	No information	Not discussed.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Low risk of bias	Data abstracted from electronic medical records by one individual.
Bias in selection of the reported result	Low risk of bias	Outcomes reported in study tables.
Overall quality assessment	**Low risk of bias**	**Low risk of bias**
Study authors	**Raman et al.**	**Raman et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	"It is possible that the association between the intervention and the outcome was not causal. Awareness of opioid risk has increased in the medical community in recent years and total opioid prescribing has begun to fall very slightly in England since 2016."
Bias in selection of participants into the study	Low risk of bias	All eligible patients were included.
Bias in classification of interventions	Low risk of bias	Intervention groups were clearly defined.
Bias due to deviations from intended interventions	No information	Not discussed.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Low risk of bias	Number of boxes of co-codamol given out by the department per month was monitored continuously throughout the intervention and recorded on run charts.

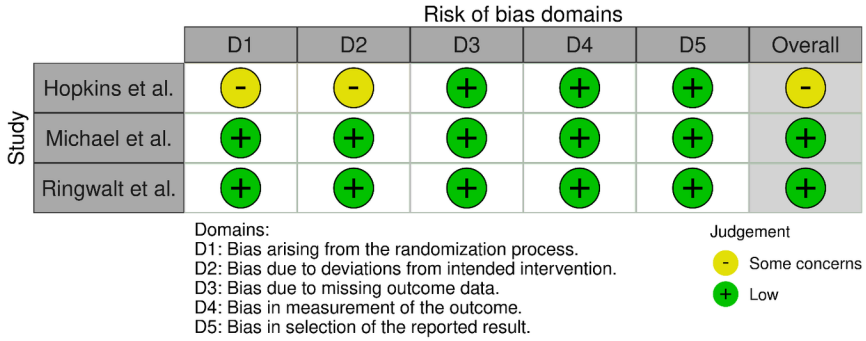
Study authors	**Andereck et al.**	**Andereck et al.**
Bias in selection of the reported result	Low risk of bias	All outcome measures reported.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Sada et al.**	**Sada et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	Potential confounding factors not addressed by experimental design or statistical analysis.
Bias in selection of participants into the study	Low risk of bias	All eligible patients were included.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention groups.
Bias due to deviations from intended interventions	No Information	Not discussed.
Bias due to missing data	Low risk of bias	Patients that were provided with an opioid prescription and refill outside the Mayo Clinic network may have been missed, however, this is the same for all intervention groups.
Bias in measurement of outcomes	Low risk of bias	Discharge opioid prescriptions were abstracted from medical records.
Bias in selection of the reported result	Low risk of bias	Outcomes reported in study tables.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Santistevan et al.**	**Santistevan et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	"Unmeasured confounders may have influenced our analysis. Factors that were not studied may have influenced opioid prescribing patterns."
Bias in selection of participants into the study	Low risk of bias	Consecutive eligible patients included in the study.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention periods.
Bias due to deviations from intended interventions	No information	Not discussed.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Low risk of bias	Retrospective chart review identifying quantity of tablets before and after intervention.
Bias in selection of the reported result	No information	Not described.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Schwab et al.**	**Schwab et al.**
Bias	**Judgement**	**Support for judgement**

Study authors	**Andereck et al.**	**Andereck et al.**
Bias due to confounding	Serious risk of bias	The authors state that "we cannot claim a causal relationship between PCA elimination and opioid reduction or increased use of non-opioid analgesics."
Bias in selection of participants into the study	Low risk of bias	All eligible patients included.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention periods.
Bias due to deviations from intended interventions	No information	Not discussed.
Bias due to missing data	Low risk of bias	Missing data not reported.
Bias in measurement of outcomes	Low risk of bias	Retrospective chart review to collect data.
Bias in selection of the reported result	No information	Not discussed.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Sigal et al.**	**Sigal et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	Potential confounding factors not addressed by experimental design or statistical analysis.
Bias in selection of participants into the study	Low risk of bias	All eligible prescriptions were included.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention periods.
Bias due to deviations from intended interventions	No information	Not discussed.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Moderate risk of bias	Retrospectively reviewed prescribing patterns.
Bias in selection of the reported result	Low risk of bias	Outcomes reported in study tables.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Stanley et al.**	**Stanley et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Low risk of bias	Potential confounding factors identified and addressed.
Bias in selection of participants into the study	Low risk of bias	All eligible patients were included in the study.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention periods.
Bias due to deviations from intended interventions	No information	Not reported.
Bias due to missing data	Low risk of bias	"Where there were missing data from the current admission record, previous admission Medical Records Online were interrogated for data."

Study authors	**Andereck et al.**	**Andereck et al.**
Bias in measurement of outcomes	Low risk of bias	Manual extraction of patient data from Medical Records Online.
Bias in selection of the reported result	Low risk of bias	Outcomes reported in study tables.
Overall quality assessment	**Low risk of bias**	**Low risk of bias**
Study authors	**Stevens et al.**	**Stevens et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	Potential confounding factors not addressed by experimental design or statistical analysis.
Bias in selection of participants into the study	Low risk of bias	All eligible patients were included.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention cycles.
Bias due to deviations from intended interventions	No information	Not discussed.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Low risk of bias	"Data for the primary objective were provided each month by the hospital pharmacy from i.Pharmacy^{TM} software."
Bias in selection of the reported result	Low risk of bias	Primary and secondary outcomes reported.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**
Study authors	**Stewart et al.**	**Stewart et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	Potential confounding factors not addressed by experimental design or statistical analysis.
Bias in selection of participants into the study	Low risk of bias	All eligible prescriptions were included.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention periods.
Bias due to deviations from intended interventions	No information	Not discussed.
Bias due to missing data	Serious risk of bias	"A substantial number of medical records requested for audit were not available."
Bias in measurement of outcomes	Serious risk of bias	"Audits were conducted retrospectively over a three-year time period by different clinical staff. Though the data collected were the same each year, interpretations of guidelines in ambiguous situations may not have been consistent."
Bias in selection of the reported result	Low risk of bias	All relevant results reported.
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**

Study authors	**Andereck et al.**	**Andereck et al.**
Study authors	**Tran et al.**	**Tran et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Low risk of bias	Potential confounding factors identified and addressed.
Bias in selection of participants into the study	Low risk of bias	All eligible patients were included.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention groups.
Bias due to deviations from intended interventions	No information	Not described.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Low risk of bias	"Doctors and pharmacists were not aware that oxycodone prescribing.
Bias in selection of the reported result	Low risk of bias	All outcomes reported.
Overall quality assessment	**Low risk of bias**	**Low risk of bias**
Study authors	**Tsega et al.**	**Tsega et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	"We must make note of a concurrent quality improvement project focused on identifying substance abuse and referral to a buprenorphine program on discharge."
Bias in selection of participants into the study	Low risk of bias	All eligible participants were included.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention groups.
Bias due to deviations from intended interventions	No information	Not described.
Bias due to missing data	Low risk of bias	No missing data reported.
Bias in measurement of outcomes	Low risk of bias	Extracted data from electronic health records and chart reviews.
Bias in selection of the reported result	Low risk of bias	Outcomes reported in article table.
Overall quality assessment	**Low risk of bias**	**Low risk of bias**
Study authors	**Villwock et al.**	**Villwock et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Low risk of bias	"Descriptive statistical analyses were performed for patient and provider demographics."
Bias in selection of participants into the study	Low risk of bias	All eligible patients included.
Bias in classification of interventions	Low risk of bias	Clear classification of intervention groups.
Bias due to deviations from intended interventions	No information	Not discussed.
Bias due to missing data	Low risk of bias	No missing data reported.

Study authors	**Andereck et al.**	**Andereck et al.**
Bias in measurement of outcomes	Low risk of bias	Prescriptions "were identified in the electronic medical record by a trained informatics specialist."
Bias in selection of the reported result	Low risk of bias	Outcomes reported in article tables and graphs.
Overall quality assessment	**Low risk of bias**	**Low risk of bias**
Study authors	**Yorkgitis et al.**	**Yorkgitis et al.**
Bias	**Judgement**	**Support for judgement**
Bias due to confounding	Serious risk of bias	No adjustment made for potential confounding factors
Bias in selection of participants into the study	Low risk of bias	All general surgery residents were invited to participate
Bias in classification of interventions	Low risk of bias	Intervention clearly classified
Bias due to deviations from intended interventions	No information	Not reported
Bias due to missing data	Low risk of bias	No missing data reported
Bias in measurement of outcomes	Serious risk of bias	General surgery residents completed an evaluation on their prescribing, which introduced bias
Bias in selection of the reported result	No information	Not reported
Overall quality assessment	**Serious risk of bias**	**Serious risk of bias**



APPENDIX 4 Quality assessment visualisation of included randomised controlled studies using the *Risk of Bias Visualisation*tool[13] (n=3)

APPENDIX 5 Quality assessment visualisation of included nonrandomised controlled studies using the *Risk of Bias Visualisation* tool[13] (n=40)