

Systematic Review

Prescriber Education Interventions to Optimize Opioid Prescribing in Acute Care: A Systematic Review

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Background: Opioid medications are frequently used effectively for analgesia in acute settings, however, they are associated with dependence and addiction, and were implicated in 47,600 American fatalities in 2017. Evidence suggests that despite guidelines and professional body recommendations, acute prescribing remains highly variable. Educational interventions targeting prescribers have potential to optimize prescribing in-line with evidence-based best practice.

Objectives: To identify the objective impacts of education interventions on opioid prescribing in the acute care setting.

Study Design: A systematic literature review.

Setting: The electronic databases MEDLINE, Embase, and Cochrane for works published until December 31, 2018. Bibliographies of relevant studies and the gray literature were also searched.

Methods: Databases were searched for interventional studies (clinical trials and pre- and poststudies). Studies describing an educational intervention delivered to clinicians and reporting at least one objective measure of opioid use in the acute care setting were included. Studies reporting only subjective outcomes and those focused on chronic pain or set in primary care were excluded. Two reviewers (RB, TB) extracted data and assessed the quality of included studies using the Downs and Black Tool.

Results: Nine studies met inclusion criteria; all used pre- and postdesigns. Three studies described stand-alone education, and the others described multifaceted interventions. All 9 interventions significantly reduced at least one of the following: high-risk agent use including meperidine use by up to 71%; total or daily dosage of opioids at discharge, including median morphine milligram equivalence (MME) from 90 mg to 45 mg per patient; and quantity of medications such as oxycodone supplied to patients, halved in one study from 6,170 expected to 2,932 supplied tablets. No increase in pain complaints or prescription refill requests were reported in those studies assessing these outcomes. The longest study examined prescribing 15 months after education delivery, reporting sustained practice changes.

Limitations: Overall study quality was fair to poor. Significant heterogeneity in settings, patient groups, methodologies, and outcomes prevented pooled quantitative analysis. No studies examined all available opioid agents or formulations.

Conclusions: These findings support prescriber education as an effective strategy to reduce opioid use and optimize prescribing in acute settings. Further research, particularly high quality randomized studies, describing the impact of education on all available opioid formulations and total MME is required. Reviewing the existing literature has offered useful models that can be implemented to improve care with opioid prescribing in acute settings.

Key words: Opioids, education, physician education, prescriber education, opioid education, opioid prescribing, systematic review, prescriptions, prevention

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Opioid misuse and overdose is an emerging problem, with 400,000 opioid-related deaths in the United States between 1999 and 2017, including 47,600 in 2017 (1,2). Although many of these figures are led by substances including illicitly manufactured fentanyl and heroin, there is concern regarding the role of prescription opioids in fatalities and in the potential transition from medical to illicit opioid use. Opioid analgesics are a mainstay of acute pain management postsurgery or injury: up to 92% of surgical patients are discharged with opioids (3,4). With opioids associated with tolerance and dependence, opioid use after injury or surgery can evolve into chronic use: patients prescribed opioids after low-risk surgery are 44% more likely to be using opioids one year later than those prescribed no opioids (5-12).

It is essential that acute opioid prescribing is optimized to reduce the risk of potential long-term addiction, while ensuring acute pain remains well-managed (13-15). Evidence-based guidelines have been developed by bodies including the American Pain Society, Centers for Disease Control and Prevention (USA), and the American Society of Anesthesiologists, and many health care organizations have developed internal policies or interventions (16-23).

However, evidence suggests prescribing remains highly variable, leading to calls for improved prescribing through a range of approaches including better opioid education in medical training (24-33). Targeted education has been shown to improve prescribing accuracy and optimize antimicrobial use among junior clinicians (34-37). In contrast, many opioid education studies have taken place in primary care or report subjective outcomes such as participant satisfaction or “preparedness” (38-40). This review evaluated objective impacts of opioid education in acute settings.

METHODS

Eligibility Criteria

English-language articles were included if they reported any interventional design to describe an educational intervention to optimize opioid prescribing in an acute setting up until December 31, 2018. Included studies reported at least one objective outcome measuring medication use or prescribing. Excluded were non-interventional studies and those targeting patients only or describing interventions without education. Studies in nonacute settings were excluded, as were those focusing on palliative or chronic pain, or substance use disorder.

Search Strategy and Study Selection

MEDLINE, Embase, and Cochrane Library were searched using keywords and database-specific subject headings: ((continuing medical OR medical OR profession* OR nurs* OR pharmac*) education) AND (opioid* OR opioid analgesi*) AND (prescrib* OR physician practice patterns OR drug utilization)). The search strategy is described in Supplement 1. Hand searching was used to find additional articles, and the gray literature was appraised using the Canadian Agency for Drugs and Technologies in Health searching tool (41). Titles and abstracts were screened for 557 identified articles meeting eligibility criteria. Among these, 21 articles were selected for full assessment, and 9 studies were selected for inclusion into the review according to inclusion criteria (Fig. 1).

This review protocol was registered in the PROSPERO international prospective register of systematic reviews (ID-CRD42018112452), which has been updated to reflect review completion.

Quality Assessment

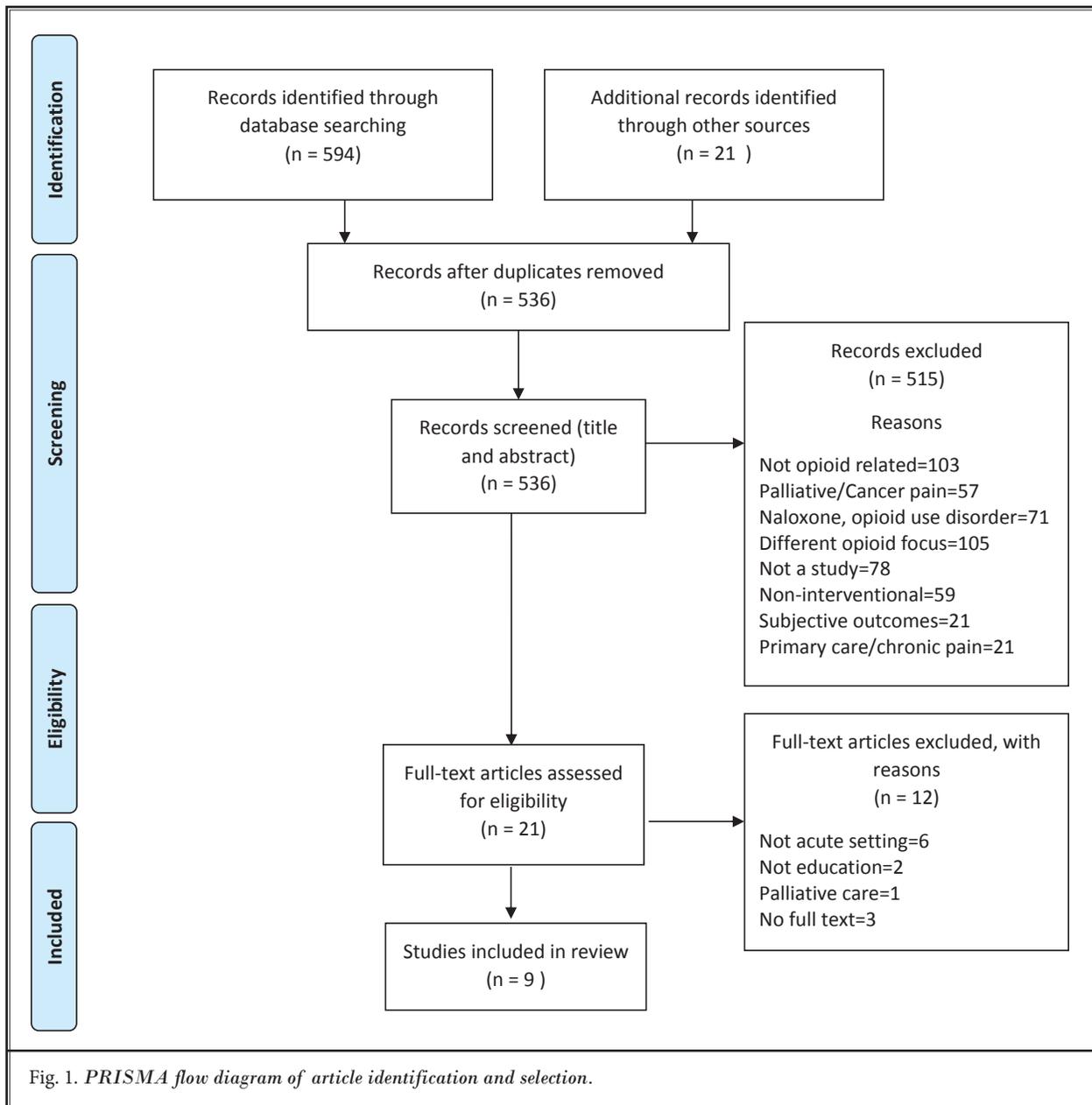
Two independent reviewers (RH, TB) evaluated study methodology and reporting quality using the Downs and Black Checklist for assessing both randomized and nonrandomized health care intervention studies (42). Using the Downs and Black Checklist, studies were assigned a score out of 29 based on the following domains: Reporting, External Validity, Bias, Confounding, and Power, with studies judged to be excellent (> 25), good (20-25), fair (15-19), and poor (< 15). This tool was selected because of the mix of study methodologies anticipated, including pre/post and other nonrandomized designs.

RESULTS

Nine studies were identified for inclusion: 6 studies were conducted in the United States and 3 studies took place in Australia. Study characteristics are described in Table 1. Two multicenter studies were conducted in the emergency department (ED) (43,44); 2 further single-site studies were based in the ED (45,46). The remaining 5 single-site studies took place in various hospital settings: one in trauma service, one in hand surgery, one in outpatient surgery, and 2 in the broader inpatient environment (47-51).

Study Quality

Overall, study quality was poor to fair; all studies used a pre- and postintervention methodology, with 2



studies employing a control group. Quality issues with internal validity including confounding and selection bias were identified. No studies randomly allocated the intervention or applied blinding to patients, data collection, or assessment of outcomes. Few studies reported multivariate analyses or described confounders such as prehospital opioid use or risk factors for opioid misuse including substance use disorder or psychiatric comorbidity. Four studies reported a priori sample size

calculations (43,45,46,50). External validity and reporting quality were otherwise satisfactory.

Interventions

Three studies described stand-alone education interventions (46,47,49). All involved the delivery of face-to-face education, however, the duration and frequency differed from a 5-minute one-off session to a one-hour bimonthly session (46,47).

Table 1. Characteristics of studies included in the review.

Author, year	Country	Quality, Score	Setting	Study design	Focus	Intervention	Participant group, sample size	Outcome measures Bold=primary
Donaldson 2017 (46)	Australia	Poor, 14	ED tertiary referral hospital	Pre/post	ED discharge, oxycodone	Education: 5-min one-on-one education by an ED physician or pharmacist to ED consultants, registrars, residents, interns, NPs MS Powerpoint and written resources	ED patients prescribed oxycodone on discharge Pre: Oct-Nov 2013, n=209 Post: Dec 2014-Feb 2015, n=592	Quality of oxycodone prescribing; dosage of oxycodone supplied; # prescriptions written; adverse effects; prescriber perceptions
Kaye 2005 (44)	Australia	Poor, 14	Multi-centre: 23 study EDs 12 control EDs	Pre/post, control group	ED use, meperidine	Multi-faceted: guidelines, posters, audits, individualised feedback, small group discussions, local opinion leaders, workshops for site co-ordinators	All opioids dispensed identified by drug safe audits Pre: Sept 2002 Post: Aug 2003; Feb 2004	% change in meperidine use; % change in morphine, tramadol, fentanyl, ketorolac use
Taylor 2007 (45)	Australia	Fair, 19	ED tertiary referral hospital	Pre/post	ED use, meperidine	Multifaceted: in-service by pharmacists to medical/nursing staff, concurrent prescribing feedback, posters in ED, memoranda on drug safes	All ED patient presentations Pre: Mar-Apr 2003, n=6785 Post: Mar-Apr 2004, n=6556	% parenteral opioid doses of meperidine; % patients given opioid receiving meperidine; % patients given parenteral opioid
Gugelmann 2017 (43)	US	Fair, 19	Multi-centre 2 EDs: referral and smaller of a tertiary network	Pre/post, 2 arms	ED discharge, oxycodone	Multifaceted: ED 1: grand round, electronic alert with risk reminder and alternatives ED 2: grand round, formal/informal nursing discussions, journal clubs, resident case discussions, electronic alert with risk reminder and alternatives	ED patients prescribed discharge pack (oxycodone-acetaminophen product) ED 1: Pre: Jan-Aug 2011 Post: Sept 2011-Aug 2012, n=45,746 ED 2: Pre: Jan-Dec 2011 Post: Jan-Aug 2012, n=71,512	Rate of opioid discharge pack prescribing; sub-analyses in "high risk" groups (<65 years, history SUD, chronic pain, psychiatric disorder)
Hill 2017 (49)	US	Fair, 17	University hospital	Pre/post	Hospital discharge, all opioids	Multi-faceted: procedure-specific recommendations for discharge quantity. Surgical grand rounds, resident general surgery meetings, emails	Opioid-naïve adults undergoing five surgeries (excl. SUD, post-op complications) Pre: Jan-Dec 2015, n=642 Post: Jun-Sept 2016, n=224	# opioid pills supplied; prescribing variability; % pills taken at follow-up; refill requests; non-opioid analgesic use
Lester 2017 (51)	US	Poor, 14	University hospital	Pre/post	Inpatient use, IM & high dose opioids	Multifaceted: grand rounds, workshops, interactive lectures, case conferences, online modules; new policies, electronic ordering defaults/alerts, opioid conversion charts, printed/electronic resources; patient resources	Nurses, pharmacists, physicians. Hospital-wide prescribing Pre-2011, Post-2013 Prescribing trends: 2011-2015	Staff knowledge (survey); % IM orders; % high dose morphine, hydromorphone, fentanyl orders

Table 1 (cont.). Characteristics of studies included in the review.

Author, year	Country	Quality, Score	Setting	Study design	Focus	Intervention	Participant group, sample size	Outcome measures Bold=primary
Oyler 2018 (47)	US	Fair, 19	University hospital	Pre/post	Hospital discharge, all opioids	Education: bimonthly hour lecture to residents; pharmacist-led presentations at MDT QA meetings; paper/web-based reference material, nursing competency assessment	Adult acute trauma patients receiving ≥1 opioid dose in hospital (excl burns, abdo/head injury, pregnant, SUD, organ failure, LOS<5 days) Pre: 2013, n=489 Post: 2015, n=424	Daily MME on discharge; inpatient opioid use; inpatient pain scores, ileus, LOS, discharge disposition
Stanek 2015 (48)	US	Poor, 14	University hospital	Pre/post	Hospital discharge, all opioids	Multifaceted: multimodal pain plan presented face-to-face to residents, faculty, fellows, nurses; policies; electronic ordering defaults; educational assist cards	Adult patients undergoing four hand operations Pre: 2011, n=63 Post: 2012, n=96; 2013, n=87	# opioid pills supplied; prescribing variability; refill requests
Ury 2002 (50)	US	Fair, 19	Private teaching hospital	Pre/post, control group	Inpatient use, meperidine	Education: case-based pain management/palliative care curriculum, 1-10 sessions.	Study: Medical patients (excl. ICU/cardiac/biliary), n=733 (pre 365, post 368) Control: Rehab/neuro patients, n=273 (pre 154, post 119) Pre: Jan-Jun 1997 Post: Jan-Jun 1999	% opioid orders for meperidine; bowel regimen use; % NSAID use

%; proportion; #: number; ED: Emergency Department; NP: nurse practitioner; NSAIDs: non-steroidal anti-inflammatory drugs; ICU: intensive care unit; SUD: substance use disorder; QA: quality assurance; LOS: length of stay; MDT: multidisciplinary team

Six studies described face-to-face education within multifaceted interventions, incorporating other responsible prescribing strategies including new guidelines or consensus recommendations, continuous auditing and individualized feedback, and changes to computerized provider order entry (CPOE) systems including standardizing supply quantities or generating alerts for high-dose orders (43-45,48,49,51).

All the education interventions were supported by visual, written, or online reference materials. Many took place within existing education delivery structures such as hospital grand rounds, journal clubs, or case presentations. Education was delivered to a range of professionals including medical interns, residents, fellows and consultants, pharmacists, and nursing staff with prescribing responsibilities including nurse practitioners and physicians' assistants.

Two studies reported attendance: Ury et al (50) reported that 100% of house clinicians attended at least one session, with 83% of staff attending the full 10-session pain management course, and Lester et al (51) reported that sessions were mandatory for house physicians.

Outcomes are reported in Table 2 and may be separated into 2 categories: evaluating in-hospital use of opioid medications and evaluating the prescribing and supply of opioids on discharge.

In-Hospital use of Opioid Medications

Five studies measured the use of opioid medications in the inpatient setting; 3 focused on meperidine.

Ury et al (50) implemented a case-based pain management curriculum for medical residents of a private US teaching hospital. The intervention was associated with a significant reduction in meperidine use from 10.4% of medical service patients to 6% ($P = 0.03$), with no change observed in the control

Table 2. Outcomes of interest for included studies.

First author, pub year	Outcomes of interest	Results
Donaldson 2017(46)	Median discharge oxycodone (dose x quantity, mg) per patient Total opioid prescriptions written	100 mg ↓ 50 mg per patient ($P = 0.04$) No sig difference*
Kaye 2005 (44)	% change in meperidine use % change in morphine, tramadol, ketorolac, fentanyl use	12 months: intervention 62% ↓ vs control 56% ↓ ($P < 0.001$) 18 months: 71% ↓ vs 64% ↓ ($P < 0.001$) 12 months: morphine 47% ↑ vs 22% ↑; tramadol 53% ↑ v 39% ↑ ketorolac/ fentanyl minimal throughout*
Taylor 2007 (45)	% parenteral opioid doses, meperidine % patients given opioids, meperidine % ED patients given parenteral opioid (morphine/meperidine)	7.2% ↓ 1.7% ($P < 0.001$) 6.3% ↓ 1.5% ($P < 0.0001$) 11.8% ↓ 11.4% ($P < 0.001$)
Gugelmann 2013 (43)	% patients receiving opioid discharge packs % 'high-risk' patients receiving opioid discharge packs	ED 1: 4.8 ↓ 2.1%, absolute reduction 2.7% (95%CI 1.8 to 3.6). ED 2: 13.9 ↓ 8.4%, absolute reduction 5.5% (95%CI 4.6 to 6.3). ≤65 years: 19.3% ↓ 12.2%; psychiatric comorbidity: 19.4% 12.2%; chronic pain: 23.7% ↓ 15.1%
Hill 2017 (49)	Mean number tablets on discharge (5 surgeries) Expected vs prescribed pills	PM: 19.8 ↓ 5.1; PMSLN: 23.7 ↓ 9.6; LC: 35.2 ↓ 19.4; LIH: 33.8 ↓ 19.3; OIH: 33.2 ↓ 18.3 (all $P < 0.0003$) Expected 6170 ↓ actual 2932, 53% reduction (post only)
Lester 2017 (51)	% parenteral orders using IM route % high dose orders: Hydromorphone ≥2mg Morphine ≥4mg Fentanyl ≥100mcg	↓ 3.6% ($P < 0.0001$) ↓ 5.2% ($P = 0.017$) ↓ 4.9% ($P < 0.0001$) ↑ 2.1% ($P = 0.016$)
Oyler 2018 (47)	Discharge daily MME % discharged with no opioids % inpatient use LA opioids	Overall: 90 mg ↓ 45 mg ($P < 0.001$); opioid-naïve: 90 mg ↓ 45 mg ($P < 0.001$); opioid-tolerant: 60 mg ↑ 75 mg ($P = 0.02$). 9% ↑ 12.7% ($P = 0.087$) 35.3% ↓ 16.5% ($P < 0.001$)
Stanek 2015 (48)	% change discharge quantities (4 surgeries)	GCE: ↓ 48% ($P = 0.02$); MCP ORIF: ↓ 20% ($P = 0.04$); DCR: ↓ 39% ($P = 0.33$); TFR: ↓ 15% ($P = 0.45$)
Ury 2002 (50)	% patients prescribed meperidine	Intervention 10.4% ↓ 6.0% ($P = 0.03$) vs control 11% ↑ 11.8% ($P = 0.85$) OR 0.55 (95%CI: 0.32 to 0.96) post-intervention

*exact numbers not reported; OR: odds ratio; ED: emergency department; MME: morphine milligram equivalence; IM: intramuscular; PM: partial mastectomy; PMSLN: partial mastectomy with sentinel lymph node biopsy; LC: laparoscopic cholecystectomy; LIH: laparoscopic inguinal hernia repair; OIH: open inguinal hernia repair; GCE: ganglion cyst excision; MCP ORIF: metacarpal open revision of fracture; DCR: dorsal compartment release; TFR: trigger finger release

group of rehabilitation and neurology patients (11.0 vs 11.8%; $P = 0.85$). Multivariate analysis demonstrated the odds of meperidine use was 45% lower in the study group postintervention (odds ratio, 0.55; 95% confidence interval (CI), 0.32 to 0.96).

Following in-services by pharmacists to medical and nursing staff, along with continuous auditing and feedback, Taylor et al (45) detected a significant

reduction in the proportion of Australian ED patients receiving parenteral opioids who received meperidine (6.3% to 1.5%; $P < 0.001$), and a reduction in the total proportion of parenteral opioid doses given that were meperidine ($P < 0.001$). In the Kaye et al (44) Australian multicenter study of 23 study hospitals and 12 control institutions, drug use evaluation was used to measure meperidine use following education interventions using

local opinion leaders and continued audit and feedback cycles. Meperidine use was decreased in the intervention group by 62% at 12 months compared to 56% in the control group ($P < 0.001$). At 18 months, 7 months following the last audit cycle, there was a total reduction of 71% compared to 64% in the control group ($P < 0.001$). In both ED studies, morphine use increased during the study period, whereas tramadol use decreased in the Taylor et al (45) study and increased in the Kaye et al (44) study. Other agents were not reported.

In the inpatient setting, Lester et al (51) reported a 3.6% reduction in the use of intramuscular opioids ($P < 0.001$), high-dose hydromorphone (≥ 2 mg, -5.2% ; $P = 0.017$), and high-dose morphine (≥ 4 mg, -4.9% ; $P < 0.001$) following a 4-year multifaceted intervention. Directed by a new pain management committee, compulsory workshops and lectures were delivered to house physicians, incorporating feedback and qualitative findings toward continuous intervention improvement. An increase in high-dose fentanyl use (≥ 100 mcg, $+2.1\%$; $P = 0.016$) was reported. The use of the included medications at lower dosages, and evaluation of other opioids or formulation such as oral oxycodone or tramadol were not reported.

Oyler et al (47) examined the effects of bimonthly lectures for surgical residents and pharmacist presentations at quality assurance meetings on both inpatient and discharge prescribing within a hospital trauma service. A significant reduction was reported in inpatients receiving long-acting opioids postintervention (35.3 vs. 16.5%; $P < 0.0001$) or intravenous patient-controlled analgesia (PCA; 39.4 vs. 17.9%; $P < 0.0001$); however, of those who did not receive PCA, median daily morphine milligram equivalence (MME) was higher (51 vs. 57 mg; $P < 0.0001$).

All of the studies evaluating inpatient opioid use reported significant changes including reductions in meperidine use, reductions in high-dose morphine, hydromorphone, and intramuscular opioid use, and reductions in long-acting opioid or PCA use after education interventions.

Prescribing and Supply of Opioid Medications at Discharge

Five studies examined the prescribing and supply of opioids at acute care discharge.

Donaldson et al (46) evaluated oxycodone quantities supplied from an Australian ED, multiplying the dosage and number of units supplied to calculate the total amount supplied per patient. A statistically signifi-

cant reduction was demonstrated from median 100 mg to 50 mg of oxycodone per patient ($P = 0.04$) following an education-only intervention delivered by ED physicians and pharmacists, with no difference in overall number of oxycodone prescriptions written.

In another ED study, Gugelmann et al (43) examined the use of prepackaged discharge analgesia packs, containing a set quantity of an oxycodone/acetaminophen combination medication, after staggered delivery of education bundles to 2 US EDs. One department received education in grand rounds plus computerized alerts at point-of-prescribing with risk reminders and suggested nonopioid alternatives. The second ED received education at grand rounds, journal clubs, and both formal and informal discussions, as well as computer alerts. The smaller bundle was associated with an absolute reduction in discharge pack prescribing of 2.7% (95% CI: 1.8, 3.6); the full bundle resulted in a reduction of 5.5% (95% CI: 4.6, 6.3). In addition, the provision of packs to patients deemed to be high risk of opioid misuse also reduced (< 65 years 19.3 vs. 12.2%; psychiatric comorbidity 19.4 vs. 12.2%; chronic pain 23.7 vs. 15.1%). Changes were sustained 8 months following the rollout; opioid prescribing outside of the discharge packs was not assessed.

Two US studies examined the number of tablets supplied postsurgery after development of procedure-specific recommendations, with education provided to clinicians at grand rounds, surgery meetings, and resident forums. Hill et al (49) demonstrated a significant reduction in tablets supplied after 5 outpatient procedures in opioid-naïve patients (partial mastectomy, partial mastectomy with lymph node biopsy, laparoscopic cholecystectomy, laparoscopic inguinal hernia repair, open inguinal hernia repair; all $P < 0.0003$). Total number of pills supplied postintervention was compared with the number expected without the intervention, with a demonstrated reduction of 53% (6,170 expected, 2,932 supplied). Stanek et al (48) demonstrated a 15% to 48% reduction in prescription size after 4 hand surgeries; 2 were statistically significant (wrist cyst excision $P = 0.02$; metacarpal fracture surgery $P = 0.04$; dorsal compartment release $P = 0.33$; trigger finger release $P = 0.45$). Follow-up evaluation at 15 months demonstrated sustained reduction in the Stanek et al (48) study.

In addition to inpatient prescribing, Oyler et al (47) evaluated the daily opioid dose prescribed at discharge for trauma patients. Following the intervention, median discharge MME halved from 90 mg to 45 mg per patient ($P < 0.001$). When opioid-naïve and

opioid-tolerant patients were separated, the reduction remained significant for opioid-naive patients; median MME increased for opioid-tolerant patients (60 to 75 mg per patient; $P = 0.02$). There was a nonsignificant increase in the total proportion of patients discharged without opioids (9% to 12.7%; $P = 0.08$).

In the 5 studies examining discharge medications, significant reductions were reported in both the quantity of tablets and the daily and total dosage of opioid medication supplied on discharge following education interventions.

Adverse Outcomes

Two studies examining discharge medication evaluated requests for additional medication (refill requests) as a follow-up measure for uncontrolled pain. Despite significant reductions in discharge prescribing, neither Stanek et al (48) nor Hill (49) et al detected an increase in refill requests. One inpatient study evaluated patient complaints and reported no increase in pain-related complaints after the intervention (43).

DISCUSSION

This systematic review identified 9 studies reporting objective outcomes following education interventions to reduce opioid prescribing. The included studies all demonstrated how education delivered to clinicians can successfully optimize various aspects of opioid prescribing including choice of opioid, dosing, routes, and quantities supplied. Different acute clinical settings included the ED, inpatient ward, and outpatient/day surgery setting. Outcomes included proportion of inpatient orders, quantity of tablets supplied, and discharge amounts expressed as MME, making comparisons between trials difficult. Previous reviews describe similar issues comparing overall effectiveness of other educational interventions on practice (34,35,52). Despite these challenges, this review demonstrates that education can significantly reduce opioid prescribing both in hospital and on discharge and identifies several themes regarding education interventions to change opioid prescribing practice.

In the majority of studies included, education was provided as part of a multifaceted intervention. This is supported by the literature; in a 2012 review of education interventions to optimize overall hospital prescribing, Brennan and Mattick (35) reported that only 7 of 64 included studies that described education-only interventions. The use of multiple concurrent strategies to inform, support, and facilitate practice change may

be more effective than a single strategy; education may be used to present or reinforce new guidelines, whereas computerized decision support tools prompt and enable best practice, or restrict prescribing within preset limits (34,53). The implementation of multiple strategies simultaneously makes evaluation of only the education facet impossible. The generalizability of the 6 studies describing multifaceted interventions may be weakened if the full complement of strategies is not implemented. Similarly, studies describing computerized decision support made use of existing electronic medication management and CPOE systems, and therefore are not applicable to all institutions.

Three studies reported significant reductions in prescribing after education-only interventions, including a 50% decrease in median discharge quantity or dose, and 45% lower odds of receiving meperidine. This demonstrates that education can still effectively influence prescribing patterns in the absence of other tools, adding to findings reported by previous reviews of prescribing education in other settings such as antimicrobial stewardship (54,55).

Format of education delivery will influence both feasibility and effectiveness of interventions. All the included studies used a face-to-face format, supplemented by online or written resources. A previous review of education interventions to improve overall prescribing practices supports the use of academic detailing, outreach education, and case-based discussions (35). Education in the identified studies was often delivered by local leaders including physicians, pharmacists, or a local pain management committee. Groh and Grimshaw (53) report that the use of outreach by experts such as pharmacists may improve the effectiveness of prescribing interventions, whereas using existing employees as opinion leaders and "champions" also removes the need for external educators, increasing feasibility.

No studies used online-only delivery of education. Despite benefits such as accessibility, further research is required to assess the effectiveness of online-only learning compared with face-to-face education. A systematic review by Liossi et al (52) of 32 studies describing online pain education resources reported that online training modules were effective at increasing knowledge, however, only 2 studies objectively measured prescribing changes, neither in acute settings.

Sustainability was observed in the 3 studies that included follow-up, with changes maintained up to 15 months after the last education intervention, however, in the presence of guideline or computer-

ized decision support (43,44,48). Educational-only interventions rely on individuals retaining and translating learning into practice. The acute hospital setting is associated with high levels of staff movement with junior clinicians rotating through specialties. Interventions targeting medical staff may rely on continuous delivery to maintain results (36,53). Using existing staff for outreach education and delivering education within established structures such as grand rounds increases the feasibility of education interventions that need repeating.

In addition to using a range of staff members to present material, education was delivered to multidisciplinary team members including medical, nursing, and pharmacy staff. Prescribing and inpatient medication charting is performed not only by medical doctors, but by nurse practitioners, physician assistants, and pharmacists. These team members may also influence medical prescribing decisions through recommendations, stewardship, and opioid deescalation (26,56).

Limitations

Limitations of Included Studies

A number of limitations were identified in the included studies. Most studies examined a specific opioid agent, route, or dose (43-46,50,51). Changes in prescribing may have flow-on effects on the use of other medications, however, only 2 studies examined use of other opioid agents, and no studies examined all available opioid medications or formulations (44,45). Future research should examine the effect of interventions on the prescribing of all available formulations to ensure that reducing use of one agent does not cause corresponding increases in other agents.

Only one study analyzed opioid-naïve and opioid-tolerant patients separately, with a second study excluding opioid-tolerant patients. For patients with acute-on-chronic pain, cessation of baseline medications in hospital may be inappropriate. It is not unexpected therefore that Oyler et al (47) found the significant reduction in opioid use in opioid-naïve patients was not mirrored in the opioid-tolerant cohort. In future studies, distinction should be made between these groups, due to differing risks and clinical needs, and to address reporting inaccuracies if analyzed together. In opioid-tolerant patients, a more appropriate outcome may be prescribing of opioids above the patient's baseline medication, measured by MME.

No studies examined dosing frequency, and only

one study examined long-acting analgesic use. Both regular dosing and long-acting formulations are associated with increased risk of dependence and chronic use, as well as increased incidence of toxicities and adverse effects, including overdose (5,57). Further evaluation of the effects of education on prescribing of long-acting or regular opioids is required because of these increased risks, as well as professional recommendations against these medications in acute pain.

Several studies focused on meperidine; global use of this agent has significantly declined due to limited advantages over other opioid medications compared with harms associated with the accumulation of normeperidine, risk of serotonin syndrome, and numerous drug interactions (19,58). However, the findings from these studies may remain translatable to other opioid medications in the same settings.

Following any practice change, potential adverse effects should be evaluated. When aiming to decrease analgesic use, it is essential that pain continues to be treated compassionately and appropriately. Only 3 studies reported refill requests or pain-related complaints to ensure that reducing opioid prescribing did not negatively affect pain management. Additional measures of pain control in acute settings could include inpatient pain scores, pain-related hospital representation, and patient-reported pain at follow-up.

Limitations of Review

This review had several limitations. Study quality was fair, with issues of internal validity and unaddressed confounding identified. No clinical trials were identified, and no studies used randomization or blinding. This is comparable to previous reviews of educational interventions (34,35). This review may be subject to publication bias; unsuccessful interventions are less likely to be reported. This review included studies from only 2 countries; no studies from low- or middle-income countries were identified. The impact of differing health services was not assessed, which may impact results. Finally, the study settings, patient groups, outcomes, and methodologies all differed to such an extent that intertrial comparisons and pooled quantitative analysis were not possible.

Despite these limitations, this review of medical education and implementation provides an important resource for those contemplating practice improvement around analgesics prescribing, as well as anyone involved in quality improvement activities by practice audit.

CONCLUSIONS

Judicious prescribing assists in reducing potential harm by minimizing the use of opioids when appropriate. The available evidence demonstrates that delivering face-to-face education to clinicians significantly and positively impacts the opioid prescribing in hospital and on discharge, reducing opioid dosages and quantities,

and influencing prescribers to avoid agents, routes, and doses associated with increased risk. Further high quality studies are required, including evaluation of all available opioid formulations and inclusion of follow-up measures of intervention sustainability and adverse effects.

Supplement 1. *Systematic review full search strategy.*

MEDLINE via OVID

Search Date: 01/30/2019		
1	exp Analgesics, Opioid/	105376
2	ANALGESIA/	18889
3	1 or 2	119863
4	EDUCATION, PROFESSIONAL/ or EDUCATION, CONTINUING/ or EDUCATION, MEDICAL, CONTINUING/ or EDUCATION, PHARMACY, CONTINUING/ or EDUCATION DEPARTMENT, HOSPITAL/ or EDUCATION, NURSING, CONTINUING/	57842
5	((doctor? or physician? or pharma\$ or surg\$ or medical) adj education\$).ti,ab.	34203
6	(continuing adj (doctor? or physician? or pharma\$ or surg\$ or medical) adj2 education\$).ti,ab.	4594
7	4 or 5 or 6	87408
8	Practice Patterns, Physicians'/ or Drug Utilization/ or INAPPROPRIATE PRESCRIBING/ or Drug Prescriptions/	89253
9	prescri*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	172400
10	8 or 9	221542
11	3 and 7 and 10	140
12	Limit 11 to English Language	135

EMBASE via OVID

Search Date: 01/30/2019		
1	analgesia/	113792
2	exp opiate/	72400
3	1 or 2	172209
4	continuing education provider/ or continuing education/ or clinical education/ or medical education/ or nursing education/ or residency education/	342240
5	(continuing adj (medical or pharma\$ or physician? or doctor? or surg\$) adj2 education\$).ti,ab.	6957
6	((doctor? or physician? or pharma\$ or surg\$ or medical) adj education\$).ti,ab.	48377
7	4 or 5 or 6	355192
8	inappropriate prescribing/	3251
9	prescri*.ti,ab.	304842
10	8 or 9	305848
11	3 and 7 and 10	365
12	limit 11 to English language	346

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Search Date: 01/30/2019		
1	MeSH descriptor: [Analgesics, Opioid] this term only	6547
2	MeSH descriptor: [Education, Continuing] explode all trees	1114
3	opioid	15874
4	(doctor or medical or surg* or pharm* or physician) education	26535
5	1 or 3	15874
6	2 or 4	26795
7	prescri*	25845
8	MeSH descriptor: [Practice Patterns, Physicians'] explode all trees	1138
9	7 or 8	26524
10	5 and 6 and 9	133
11	Filter 10 by Protocol or Trial	76

REFERENCES

1. Gomes T, Tadrous M, Mamdani MM, Paterson J, Juurlink DN. The burden of opioid-related mortality in the united states. *JAMA Network Open* 2018; 1:e180217.
2. Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G. Drug and opioid-involved overdose deaths—United States, 2013–2017. *MMWR Morb Mortal Wkly Rep* 2019; 67:1419–2027.
3. Fujii MH, Hodges AC, Russell RL, et al. Post-discharge opioid prescribing and use after common surgical procedure. *J Am Coll Surg* 2018; 226:1004–1012.
4. Colton IB, Fujii MH, Ahern TP, et al. Postoperative opioid prescribing patterns after vascular surgery. *J Vasc Surg* 2017; 66:e8.
5. Deyo RA, Hallvik SE, Hildebran C, et al. Association between initial opioid prescribing patterns and subsequent long-term use among opioid-naive patients: A statewide retrospective cohort study. *J Gen Intern Med* 2017; 32:21–27.
6. Maree RD, Marcum ZA, Saghabi E, Weiner DK, Karp JF. A systematic review of opioid and benzodiazepine misuse in older adults. *Am J Geriatr Psychiatry* 2016; 24:949–963.
7. Passik SD. Issues in long-term opioid therapy: Unmet needs, risks, and solutions. *Mayo Clin Proc* 2009; 84:593–601.
8. Clarke H, Soneji N, Ko DT, Yun L, Wijesundera DN. Rates and risk factors for prolonged opioid use after major surgery: Population based cohort study. *BMJ* 2014; 348:g1251.
9. Calcaterra SL, Yamashita TE, Sung-Joon M, Keniston A, Frank JW, Binswanger IA. Opioid prescribing at hospital discharge contributes to chronic opioid use. *J Gen Intern Med* 2016; 31:478–485.
10. Alam A, Gomes T, Zheng H, Mamdani MM, Juurlink DN, Bell CM. Long-term analgesic use after low-risk surgery: A retrospective cohort study. *Arch Intern Med* 2012; 172:425–430.
11. Macintyre PE, Huxtable CA, Flint SL, Dobbin MD. Costs and consequences: A review of discharge opioid prescribing for ongoing management of acute pain. *Anaesth Intensive Care* 2014; 42:558–574.
12. Zee AV. The promotion and marketing of oxycontin: Commercial triumph, public health tragedy. *Am J Public Health* 2009; 99:221–227.
13. Soffin EM, Waldman SA, Stack RJ, Liguori GA. An evidence-based approach to the prescription opioid epidemic in orthopedic surgery. *Anesth Analg* 2017; 125:1704–1713.
14. Hill MV, Stucke RS, Billmeier SE, Kelly JL, Barth RJ Jr. Guideline for discharge opioid prescriptions after inpatient general surgical procedures. *J Am Coll Surg* 2018; 226:996–1003.
15. Overton HN, Hanna MN, Bruhn WE, et al. Opioid-prescribing guidelines for common surgical procedures: An expert panel consensus. *J Am Coll Surg* 2018; 227:411–418.
16. Frieden TR, Houry D. Reducing the risks of relief—the CDC opioid-prescribing guideline. *N Engl J Med* 2016; 374:1501–1504.
17. Webster L. Eight principles for safer opioid prescribing. *Pain Med* 2013; 14:959–961.
18. Scully RE, Schoenfeld AJ, Jiang W, et al. Defining optimal length of opioid pain medication prescription after common surgical procedures. *JAMA Surg* 2018; 153:37–43.
19. Schug S, Palmer G, Scott D, Halliwell R, Trinca J. *Acute Pain Management: Scientific Evidence*. 4th ed. Melbourne, Australia: ANZCA & FPM; 2015.
20. Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of postoperative pain: A clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *Pain* 2016; 17:131–157.
21. MacLean CD, Fujii M, Ahern TP, et al. Impact of policy interventions on postoperative opioid prescribing. *Pain Med* 2018 Nov 8. [Epub ahead of print].
22. Wetzel M, Hockenberry J, Raval MV. Interventions for postsurgical opioid prescribing: A systematic review of interventions for postsurgical opioid prescribing. *JAMA Surg* 2018; 153:948–954.
23. Meisenberg BR, Grover J, Campbell C, Korpon D. Assessment of opioid prescribing practices before and after implementation of a health system intervention to reduce opioid overprescribing. *JAMA Netw Open* 2018; 1:e182908.
24. Hill VM, McMahon LM, Stucke SR, Barth JR. Wide variation and excessive dosage of opioid prescriptions for common general surgical procedures. *Ann Surg* 2017; 265:709–714.
25. Karanges EA, Blanch B, Buckley NA, Pearson SA. Twenty-five years of prescription opioid use in Australia: A whole-of-population analysis using pharmaceutical claims. *Br J Clin Pharmacol* 2016; 82:255–267.
26. Bui T, Konstantos A, Dooley M. *Implementation of the Analgesic Stewardship Pharmacist Role. Medicines Management*. Sydney, Australia: Society of Hospital Pharmacists of Australia; 2017.
27. Feinberg AE, Chesney TR, Srikandarajah S, Acuna SA, McLeod RS. Opioid use after discharge in postoperative patients: A systematic review. *Ann Surg* 2018; 267:1056–1062.
28. Chen EY, Marcantonio A, Tornetta P 3rd. Correlation between 24-hour pre-discharge opioid use and amount of opioids prescribed at hospital discharge. *JAMA Surg* 2018; 153:e174859.
29. Gordon DB, de Leon-Casasola OA, Wu CL, Sluka KA, Brennan TJ, Chou R. Research gaps in practice guidelines for acute postoperative pain management in adults: Findings from a review of the evidence for an American Pain Society clinical practice guideline. *Pain* 2016; 17:158–166.
30. Khidir H, Weiner SG. A call for better opioid prescribing training and education. *West J Emerg Med* 2016; 17:686–689.
31. Barth KS, Guille C, McCauley J, Brady KT. Targeting practitioners: A review of guidelines, training, and policy in pain management. *Drug Alcohol Depend* 2017; 173(Suppl 1):S22–S30.
32. Webster F, Bremner S, Oosenbrug E, Durant S, McCartney CJ, Katz J. From opioidphobia to overprescribing: A critical scoping review of medical education training for chronic pain. *Pain Med* 2017; 18:1467–1475.
33. Cushman PA, Liebschutz JM, Hodgkin JG, et al. What do providers want to know about opioid prescribing? A qualitative analysis of their questions. *Subst Abuse* 2017; 38:222–229.
34. Ross S, Loke YK. Do educational interventions improve prescribing by medical students and junior doctors? A systematic review. *Br J Clin Pharmacol* 2009; 67:662–670.
35. Brennan N, Mattick K. A systematic review of educational interventions to change behaviour of prescribers in hospital settings, with a particular emphasis on new prescribers. *Br J Clin Pharmacol* 2013; 75:359–372.

36. Pulcini C, Gyssens IC. How to educate prescribers in antimicrobial stewardship practices. *Virulence* 2013; 4:192-202.
37. Davey P, Marwick CA, Scott CL, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev* 2017; 2:CD003543.
38. Roth CS, Burgess DJ. Changing residents' beliefs and concerns about treating chronic noncancer pain with opioids: Evaluation of a pilot workshop. *Pain Med* 2008; 9:890-902.
39. Young A, Alfred KC, Davignon PP, Hughes LM, Robin LA, Chaudhry HJ. Physician survey examining the impact of an educational tool for responsible opioid prescribing. *J Opioid Manag* 2012; 8:81-87.
40. Zisblatt L, Hayes SM, Lazure P, Hardsy I, White JL, Alford DP. Safe and competent opioid prescribing education: Increasing dissemination with a train-the-trainer program. *Subst Abuse* 2017; 38:168-176.
41. Canadian Agency for Drugs and Technologies in Health. *Grey Matters: A Practical Tool for Searching Health-Related Grey Literature*. Ottawa, Canada: CADTH; 2018.
42. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health* 1998; 52:377-384.
43. Gugelmann H, Shofer FS, Meisel ZF, Perrone J. Multidisciplinary intervention decreases the use of opioid medication discharge packs from 2 urban EDs. *Am J Emerg Med* 2013; 31:1343-1348.
44. Kaye KI, Welch SA, Graudins LV, et al. Meperidine in emergency departments: Promoting evidence-based prescribing. *Med J Aust* 2005; 183:129-133.
45. Taylor SE, Braitberg G, Lugt J. Multifaceted education initiative minimizes meperidine prescribing in the emergency department. *Emerg Med Australas* 2007; 19:25-30.
46. Donaldson SR, Harding AM, Taylor SE, Vally H, Greene SL. Evaluation of a targeted prescriber education intervention on emergency department discharge oxycodone prescribing. *Emerg Med Australas* 2017; 29:400-406.
47. Oyler D, Bernard A, VanHoose J, et al. Minimising opioid use after acute major trauma. *Am J Health Syst Pharm* 2018; 75:105-110.
48. Stanek JJ, Renslow MA, Kalliainen LK. The effect of an educational program on opioid prescription patterns in hand surgery: A quality improvement program. *J Hand Surg Am* 2015; 40:341-346.
49. Hill VM, Stucke SR, McMahon LM, Beeman LJ, Barth JR. An educational intervention decreases opioid prescribing after general surgical operations. *Ann Surg* 2018; 267:468-472.
50. Ury WA, Rahn M, Tolentino V, et al. Can a pain management and palliative care curriculum improve the opioid prescribing practices of medical residents? *J Gen Intern Med* 2002; 17:625-631.
51. Lester PE, Shehata J, Fazzari M, Islam S. Impact of hospital-wide comprehensive pain management initiatives. *Am J Med Qual* 2017; 32:591-597.
52. Lioffi C, Failo A, Schoth DE, Williams G, Howard RF. The effectiveness of online pain resources for health professionals: A systematic review with subset meta-analysis of educational intervention studies. *Pain* 2018; 159:631-643.
53. Grol R, Grimshaw J. From best evidence to best practice: Effective implementation of change in patients' care. *Lancet* 2003; 362:1225-1230.
54. Davis DA, Thomson M, Oxman AD, Haynes R. Changing physician performance: A systematic review of the effect of continuing medical education strategies. *JAMA* 1995; 274:700-705.
55. Davis MT, Bateman B, Avorn J. Educational outreach to opioid prescribers: The case for academic detailing. *Pain Physician* 2017; 20:S147-S151.
56. Tran T, Taylor SE, Hardidge A, Findakly D, Aminian P, Elliott RA. Impact of pharmacists assisting with prescribing and undertaking medication review on oxycodone prescribing and supply for patients discharged from surgical wards. *J Clin Pharm Ther* 2017; 42:567-572.
57. Shah A, Hayes CJ, Martin BC. Characteristics of initial prescription episodes and likelihood of long-term opioid use—United States, 2006-2015. *MMWR Morb Mortal Wkly Rep* 2017; 66:265-269.
58. Friesen KJ, Falk J, Bugden S. The safety of meperidine prescribing in older adults: A longitudinal population-based study. *BMC Geriatr* 2016; 16:100.